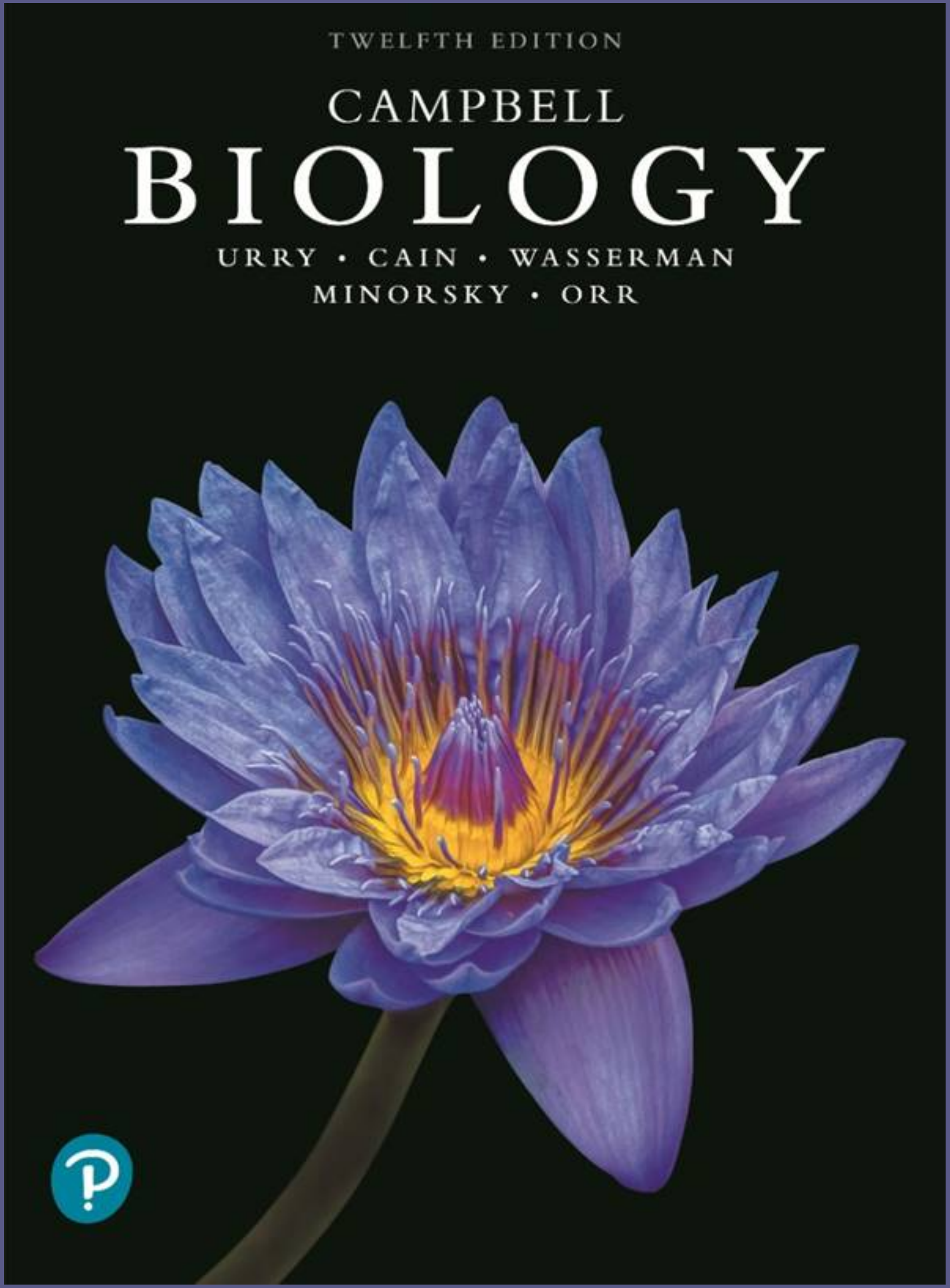


Chapter 48

Neurons, Synapses, and Signaling

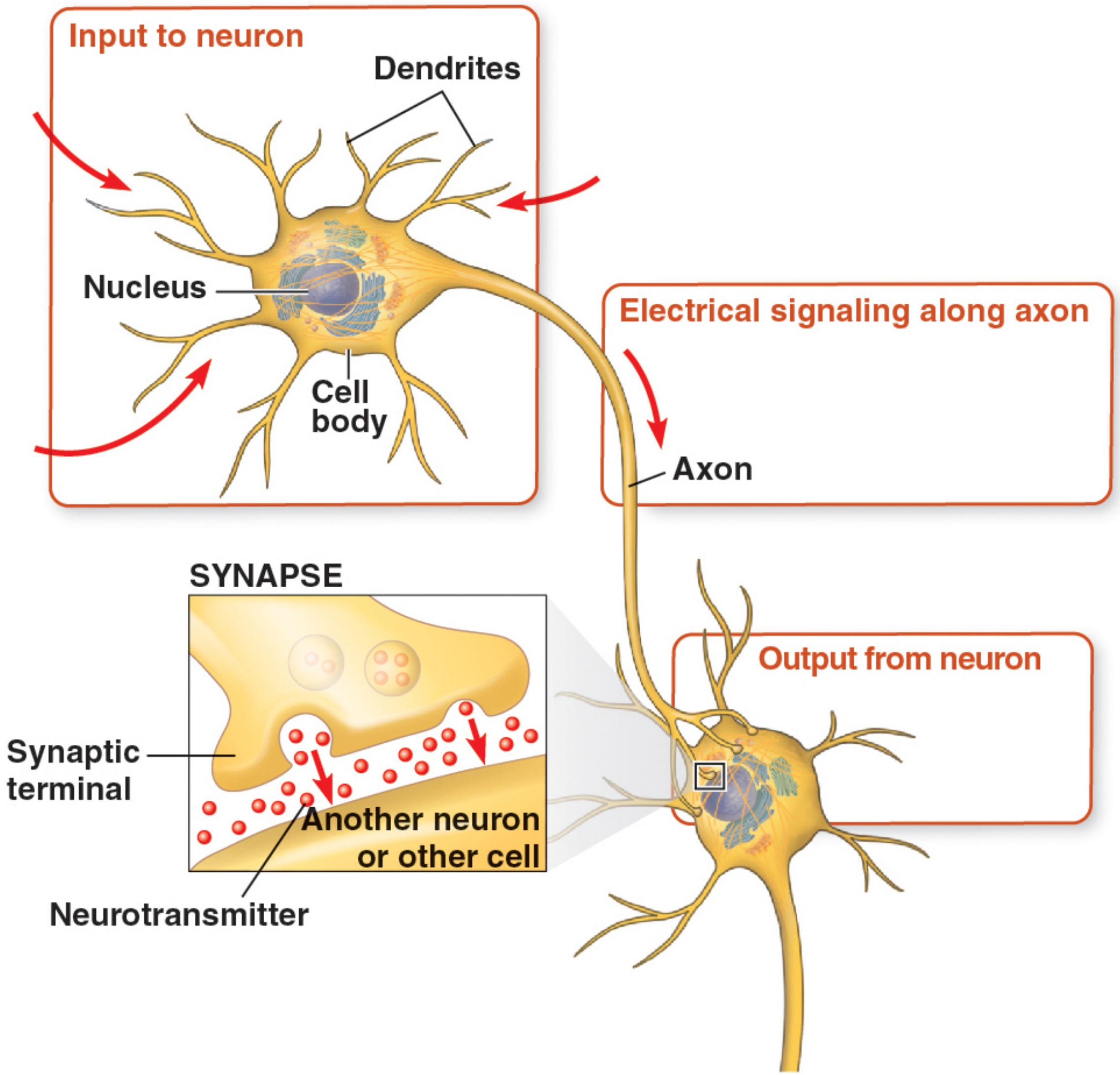
Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

Figure 48.1a

Figure 48.1b

How does a neuron transmit information?

A neuron receives information, transmits it along an axon, and transmits the information to other cells via synapses.



CONCEPT 48.1: Neuron structure and organization reflect function in information transfer

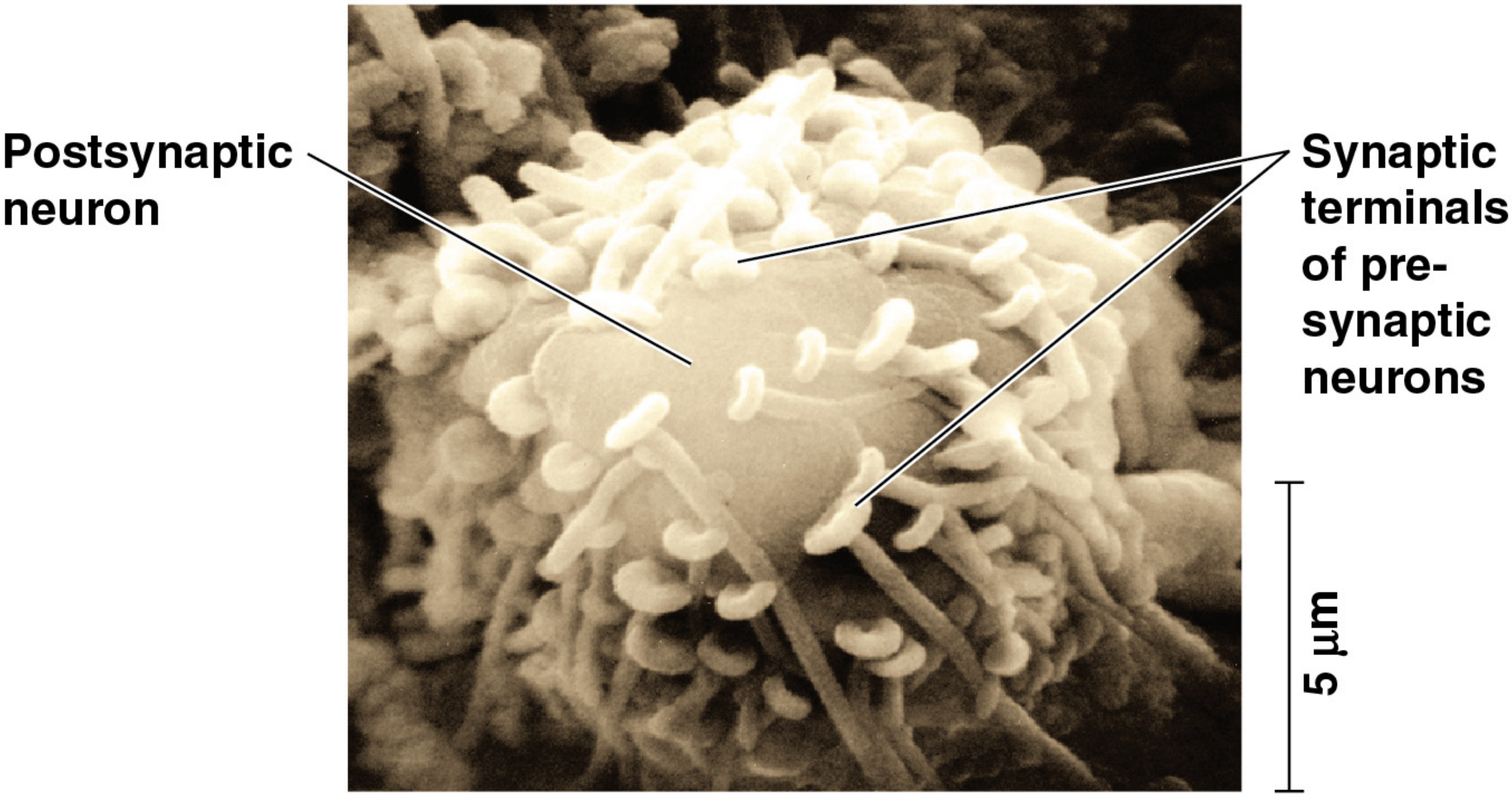
- The **neuron** is a cell that exemplifies the close fit between form and function

Neuron Structure and Function

- Most of a neuron’s organelles are in the **cell body**
- Most neurons have **dendrites**, highly branched extensions that receive signals from other neurons
- The **axon** is often a much longer extension that transmits signals to other cells at synapses
- The cone-shaped base of an axon is called the axon hillock

- A **synapse** is a junction between an axon and another cell
- The part of each axon branch that forms this junction is a synaptic terminal
- At most synapses, chemical messengers called **neurotransmitters** pass information from the transmitting neuron to the receiving cell

Figure 48.2


Postsynaptic neuron
Synaptic terminals of pre-synaptic neurons
5 µm

Lines of Communication

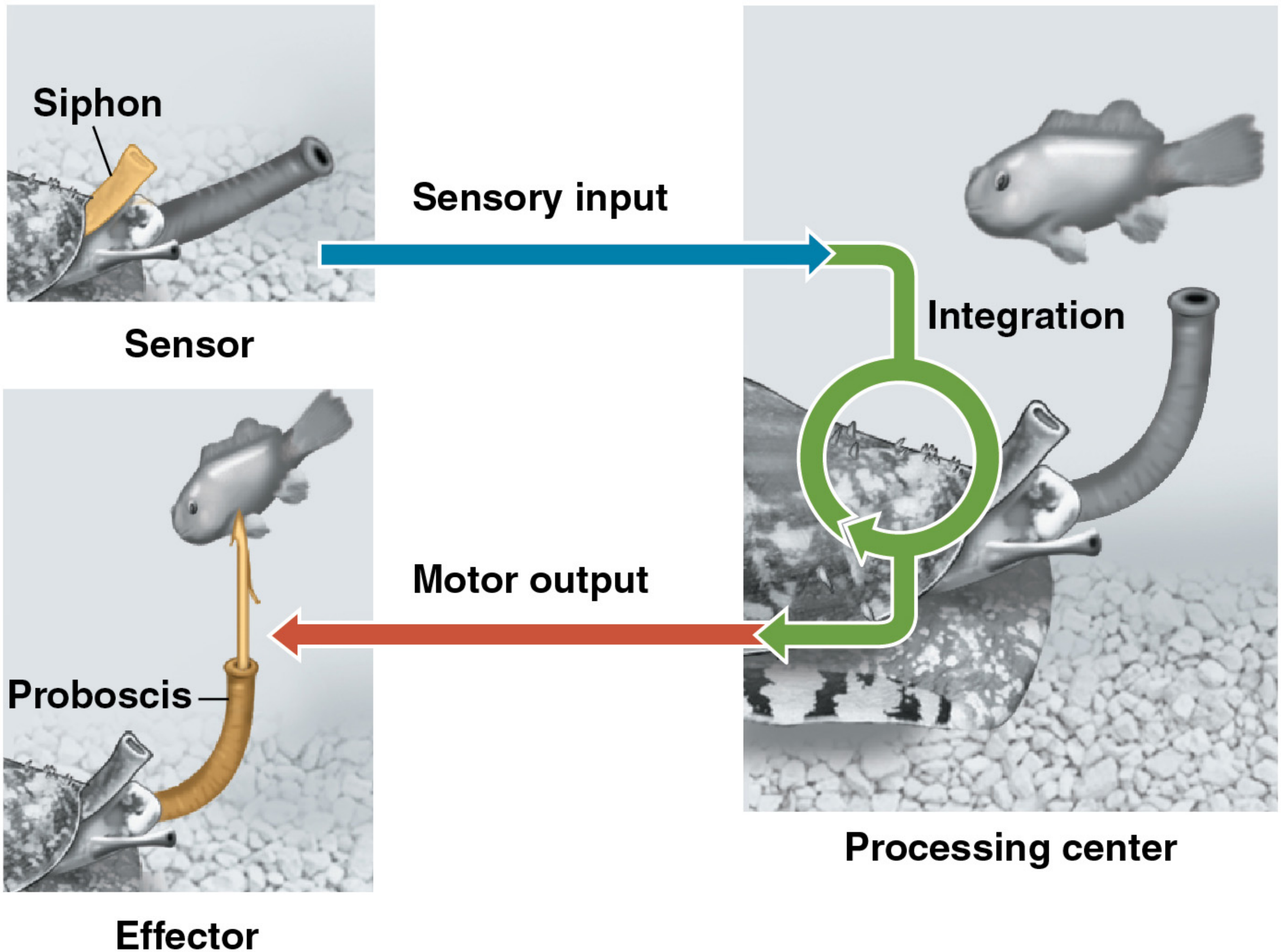
- The cone snail kills prey with venom that disables neurons
- **Neurons** are nerve cells that transfer information within the body
- Neurons use two types of signals to communicate: electrical signals (long-distance) and chemical signals (short-distance)

Introduction to Information Processing

- Nervous systems process information in three stages: sensory input, integration, and motor output
- In all but the simplest animals, specialized populations of neurons handle each stage of information processing

- **Sensory neurons** transmit information about external stimuli such as light, touch, or smell
- **Interneurons** integrate (analyze and interpret) the information
- **Motor neurons** transmit signals to muscle cells, causing them to contract

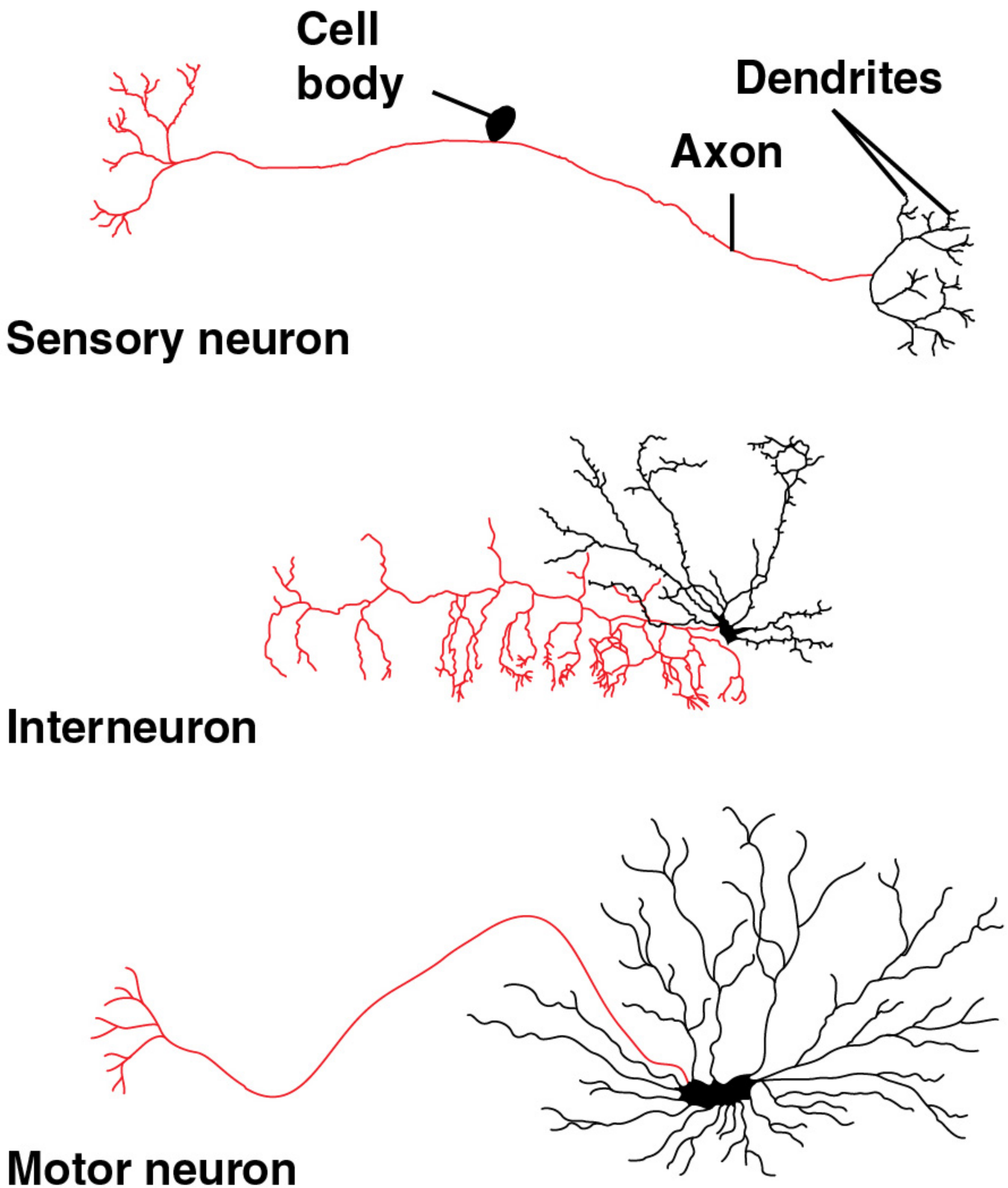
Figure 48.3



Siphon
Sensory input
Integration
Sensor
Motor output
Proboscis
Processing center
Effector

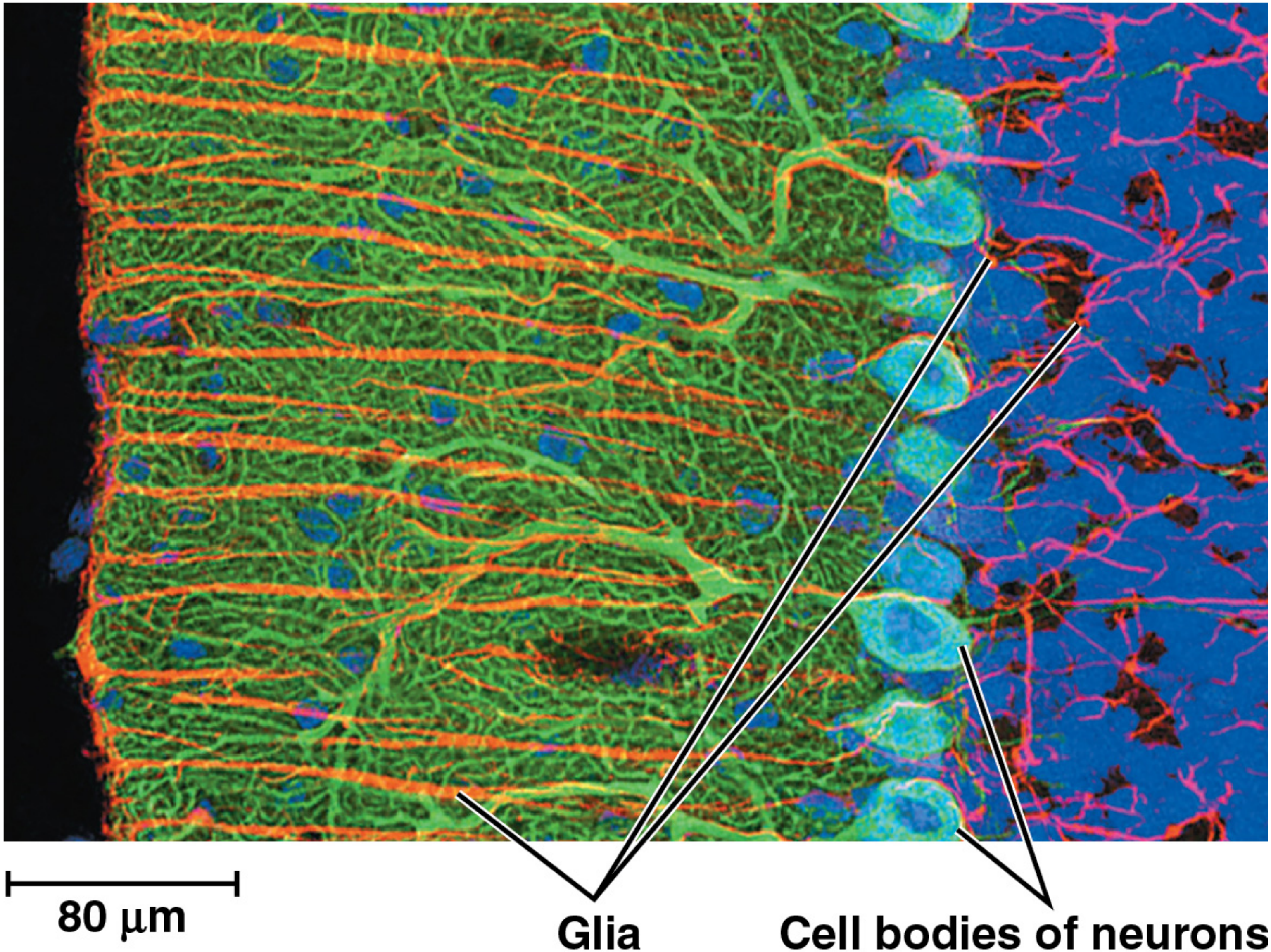
- Interpreting signals in the nervous system involves sorting a complex set of paths and connections
- The shape of a neuron can vary from simple to quite complex, depending on its role in information processing
- When grouped together, the axons of neurons form bundles we call **nerves**

Figure 48.4

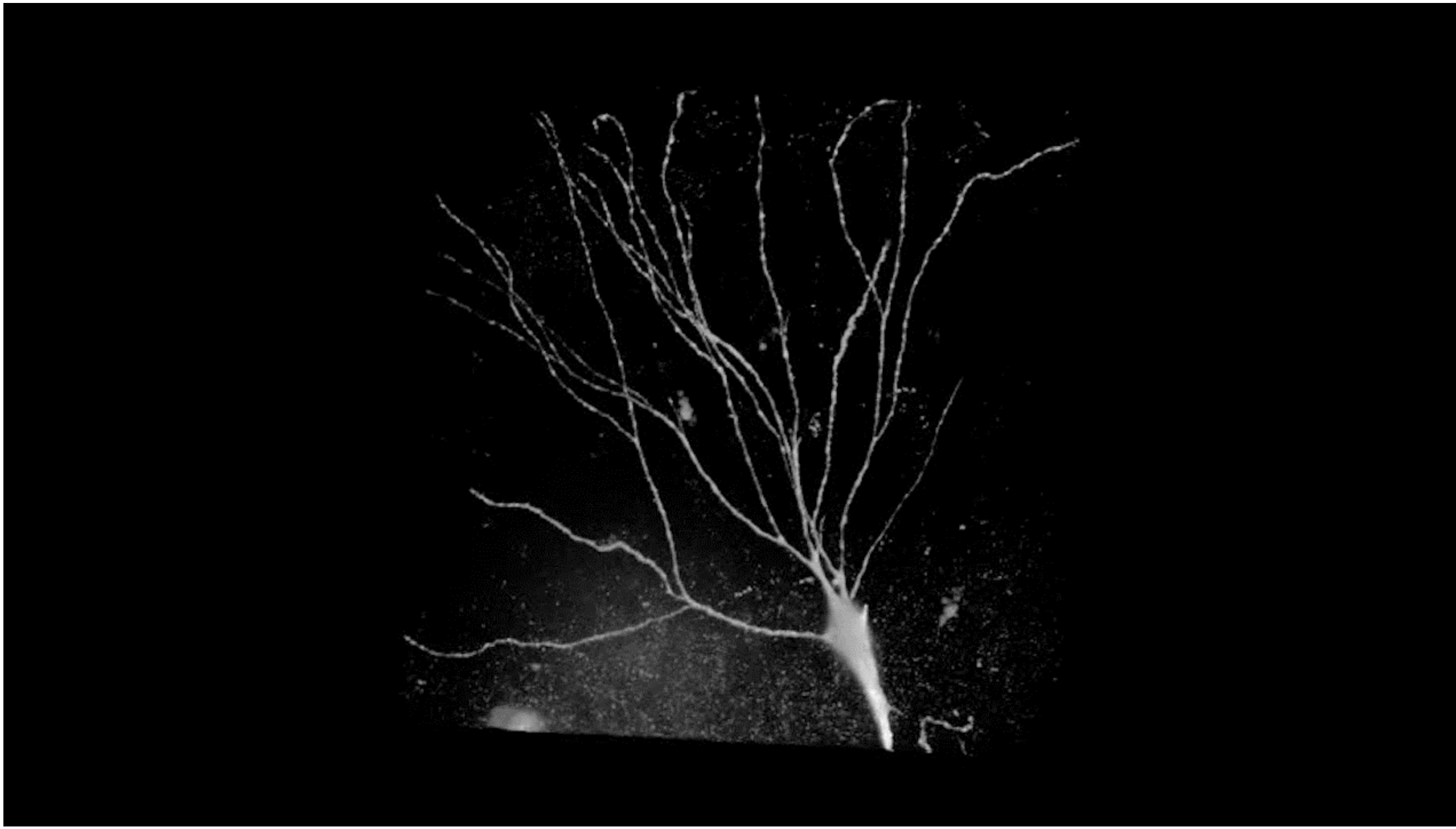

Cell
body
Dendrites
Axon
Sensory neuron
Interneuron
Motor neuron

- Many animals have a complex nervous system that consists of
  - A **central nervous system (CNS)**, where integration takes place; this includes the **brain** or simpler clusters called **ganglia**
  - A **peripheral nervous system (PNS)**, which carries information into and out of the CNS
  - Neurons of both the CNS and PNS require supporting cells called glial cells, or **glia**

Figure 48.5



Video: Dendrites of a Neuron



CONCEPT 48.2: Ion pumps and ion channels establish the resting potential of a neuron

- Every cell has a voltage (difference in electrical charge) across its plasma membrane called a **membrane potential**
- The **resting potential** is the membrane potential of a neuron that is not sending signals
- Changes in membrane potential are called action potentials

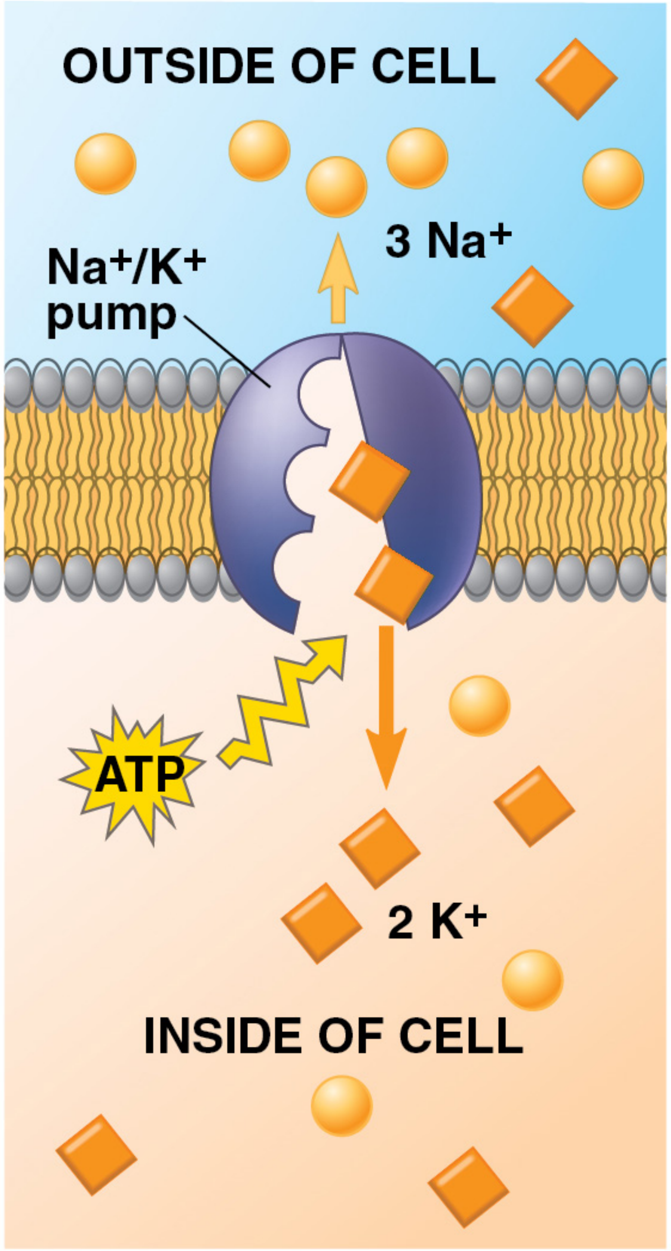
Formation of the Resting Potential

- In most neurons, the concentration of K^+ is higher inside the cell, while the concentration of Na^+ is higher outside the cell
- **Sodium-potassium pumps** use the energy of ATP to transport into the cell K^+ and Na^+ out of the cell
- This maintains the concentration gradient across the membrane

Table 48.1 Ion Concentrations Inside and Outside of Mammalian Neurons

Ion	Intracellular Concentration (m*M*)	Extracellular Concentration (m*M*)
Potassium (K^+)	140	5
Sodium (Na^+)	15	150
Chloride (Cl^-)	10	120
Large anions (A^-), such as proteins, inside cell	100	Not applicable

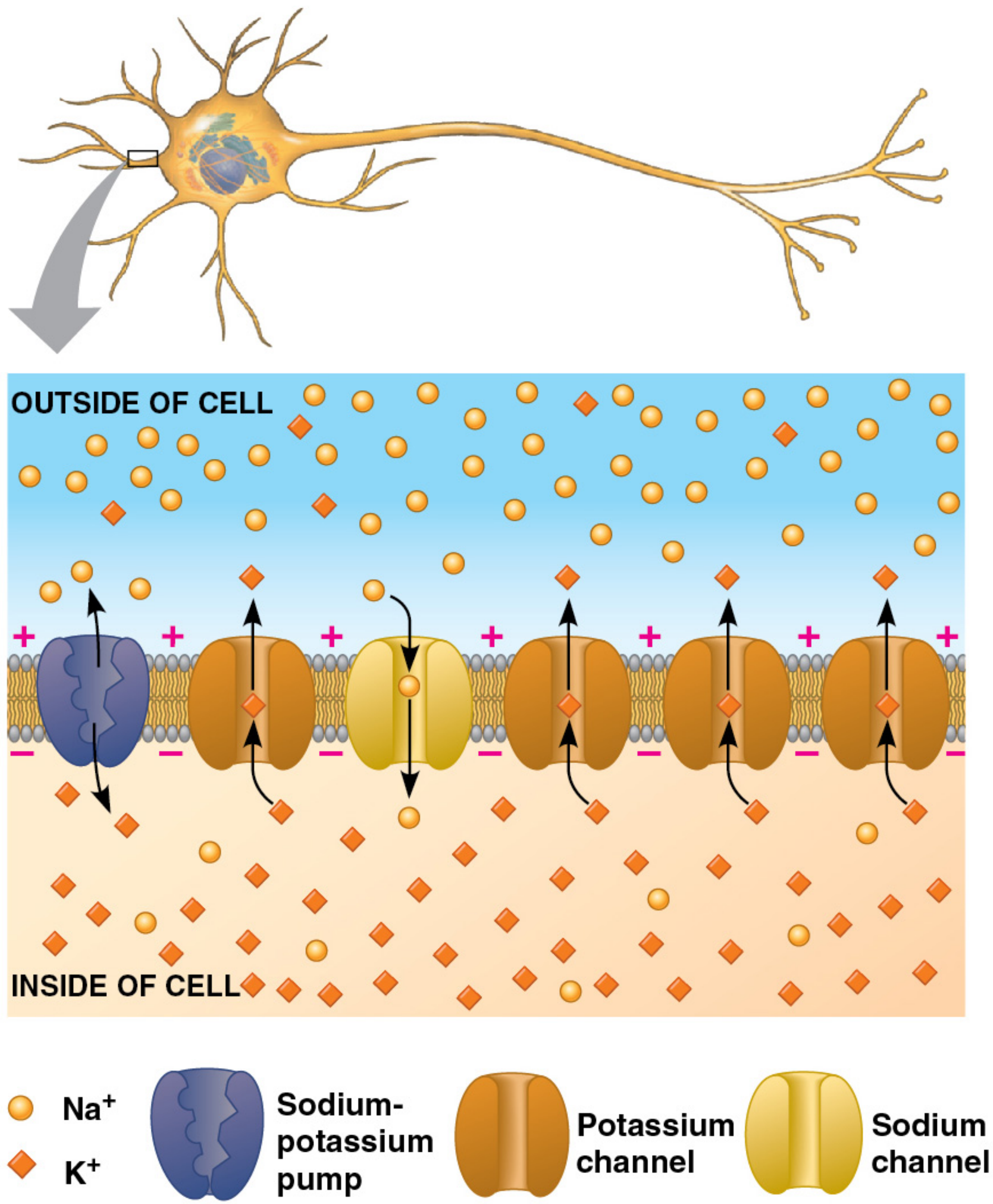
Figure 48.6



- **Ion channels** are pores that span the plasma membrane, and allow ions to diffuse back and forth across the membrane
- Concentration gradients of ions across a membrane represent a form of potential energy that can be harnessed for cellular processes
- Ion channels convert this chemical potential energy to electrical potential energy, through selective permeability, allowing only certain ions to diffuse across the membrane

- A neuron at resting potential contains many open K^+ channels and fewer open Na^+ channels; K^+ diffuses out of the cell
- The resulting buildup of negative charge within the neuron is the major source of membrane potential

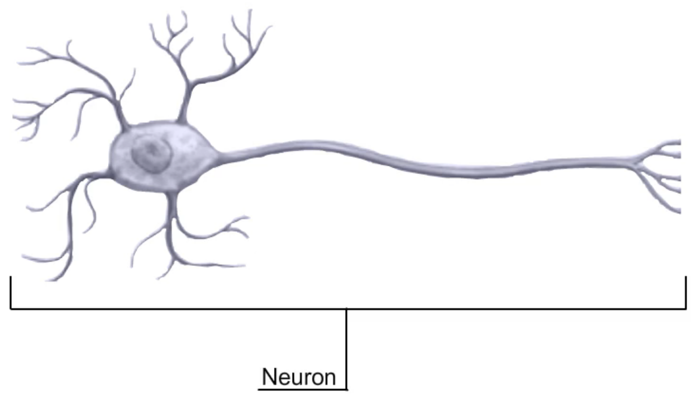
Figure 48.7


OUTSIDE OF CELL
INSIDE OF CELL
+
−
Na+
K+
Sodium-potassium pump
Potassium channel
Sodium channel

Animation: Membrane Potentials

Membrane Potentials

Membrane Potentials and Channels



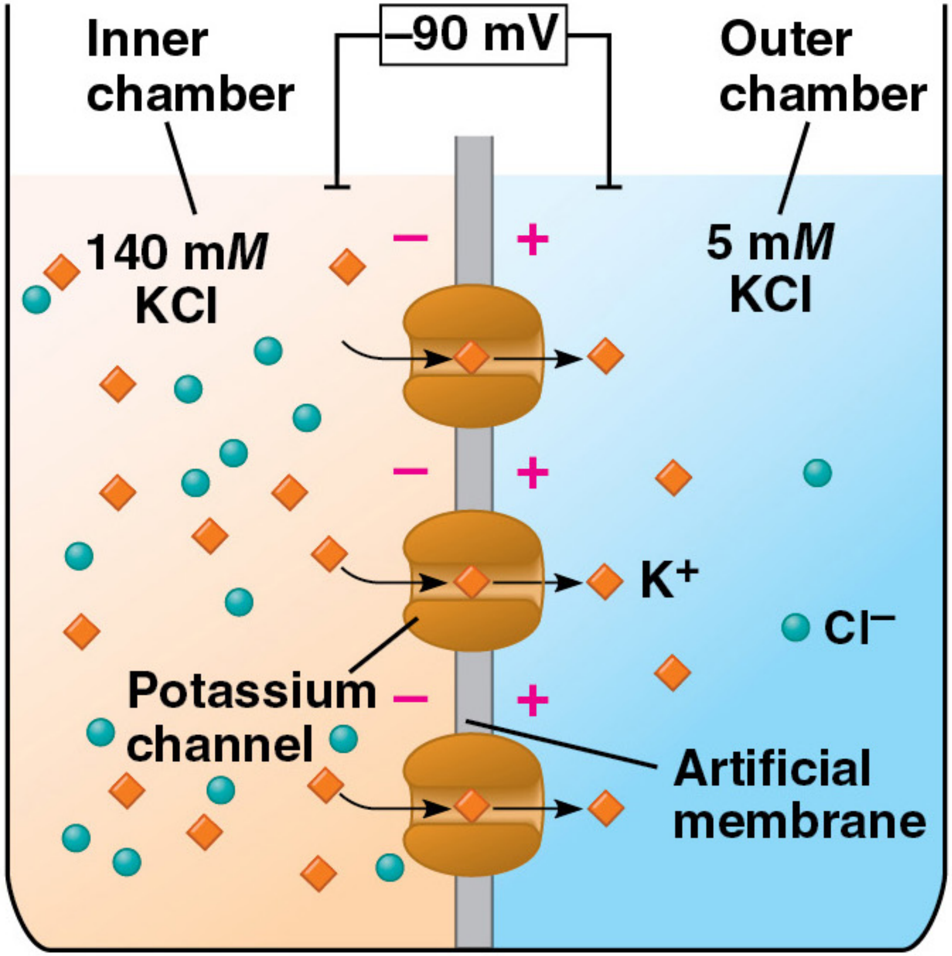
[redacted]

BioFlix® Animation: Resting Potential

Modeling the Resting Potential

- Resting potential can be modeled by an artificial membrane that separates two chambers
  - The concentration of KCl is higher in the inner chamber and lower in the outer chamber
  - K^+ diffuses down its gradient to the outer chamber
  - Negative charge (Cl^-) builds up in the inner chamber
- At equilibrium, both the electrical and chemical gradients are balanced

Figure 48.8a



(a) Membrane selectively permeable to K^+

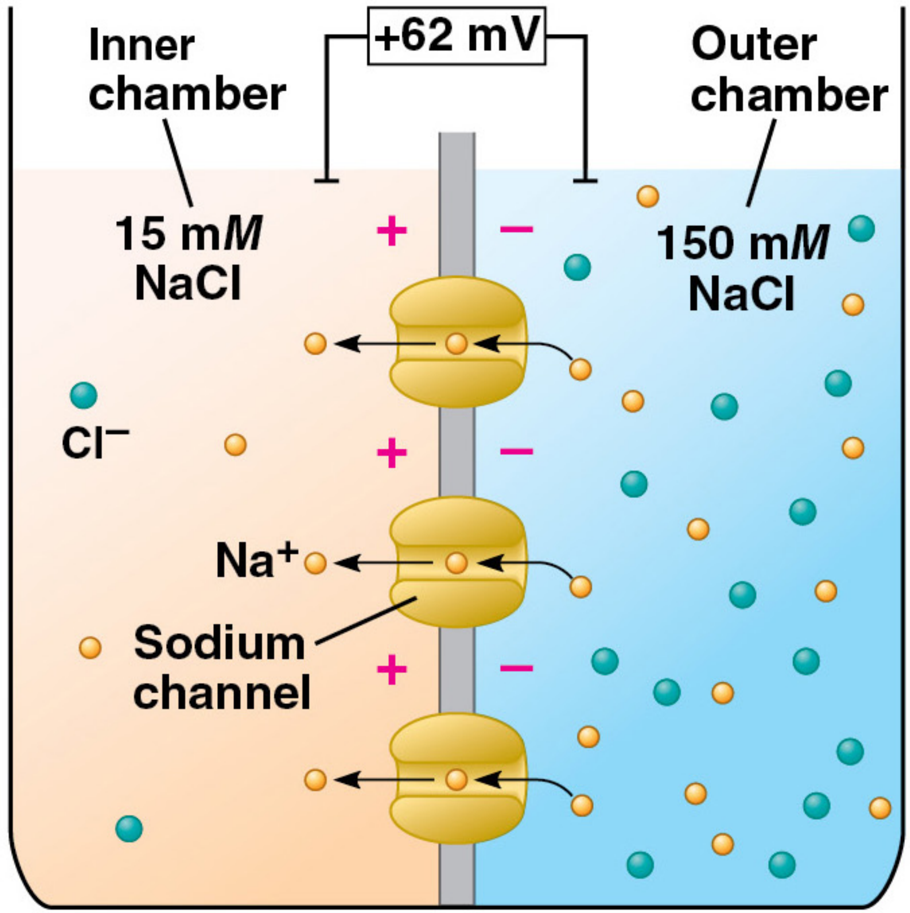
$$E_K = 62\ \text{mV}\left(\log \frac{5\ \text{m}M}{140\ \text{m}M}\right) = -90\ \text{mV}$$

- **The equilibrium potential (E_{ion})** is the membrane voltage for a particular ion at equilibrium and can be calculated using the Nernst equation:

$$E_{\text{ion}} = 62\ \text{mV}\ (\log([\text{ion}]_{\text{outside}} / [\text{ion}]_{\text{inside}}))$$

- The equilibrium potential of K^+ (E_K) is negative, while the equilibrium potential of Na^+ (E_{Na}) is positive

Figure 48.8b



(b) Membrane selectively permeable to Na^+

$$E_{Na} = 62\ \text{mV}\left(\log\frac{150\ \text{m}M}{15\ \text{m}M}\right) = +62\ \text{mV}$$

- In a resting neuron, the currents of K^+ and Na^+ are equal and opposite, and the resting potential across the membrane remains steady

CONCEPT 48.3: Action potentials are the signals conducted by axons

- Intracellular recording can be used to monitor the changes in membrane potential
- Changes in membrane potential occur because neurons contain **gated ion channels** that open or close in response to stimuli
- **Voltage-gated ion channels** open or close in response to a change in voltage across the plasma membrane of the neuron

Figure 48.9

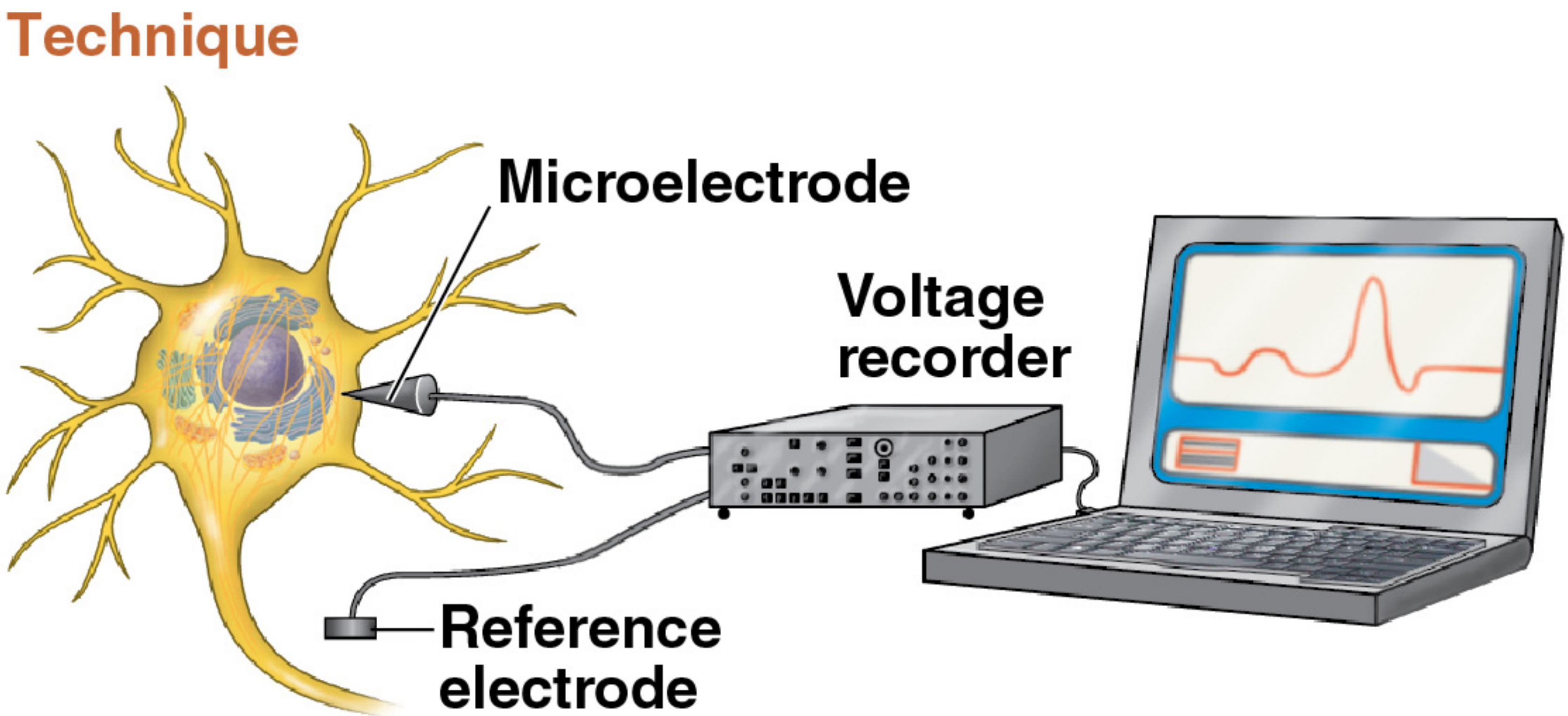
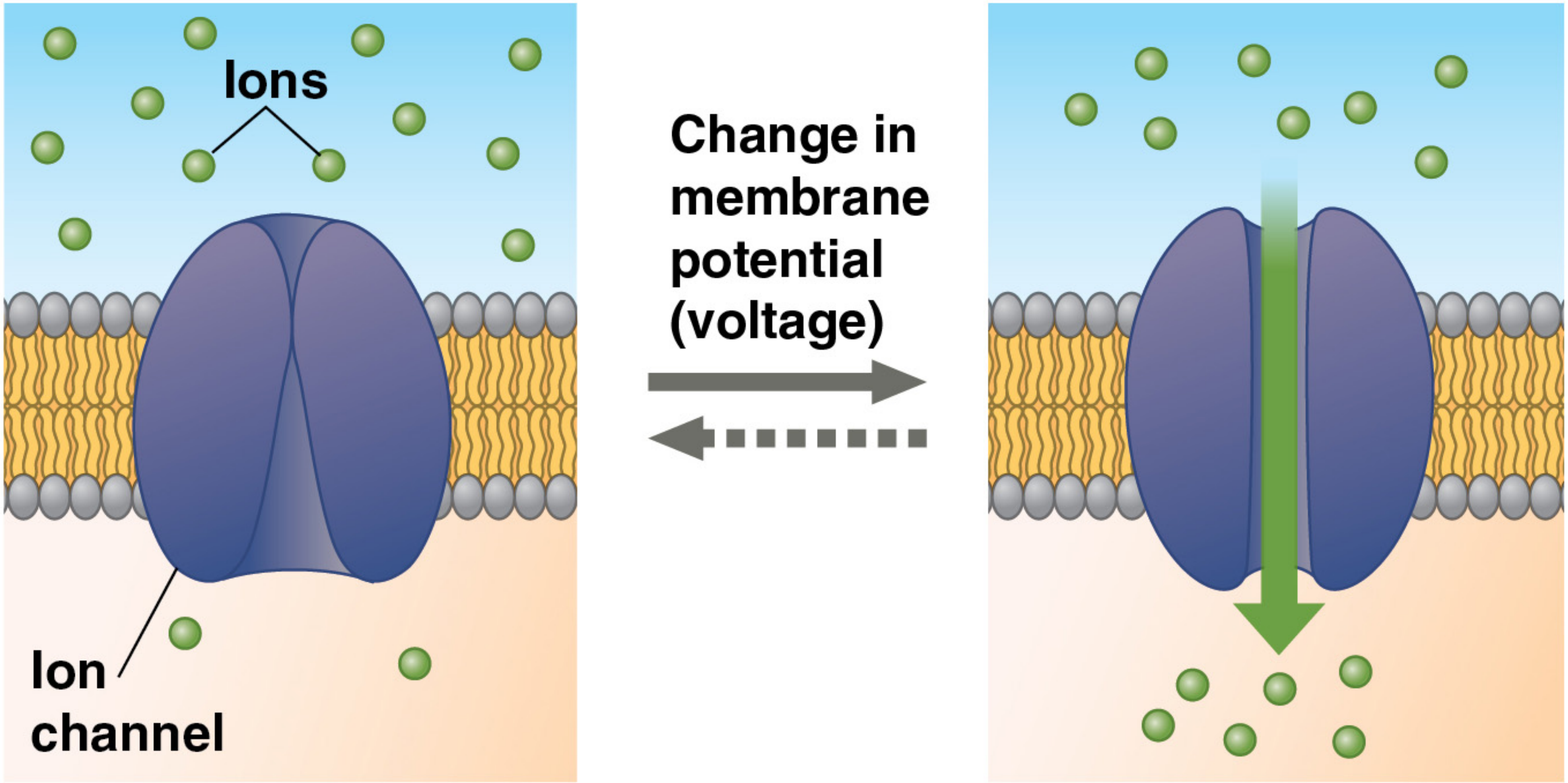

Technique
Microelectrode
Voltage recorder
Reference electrode

Figure 48.10



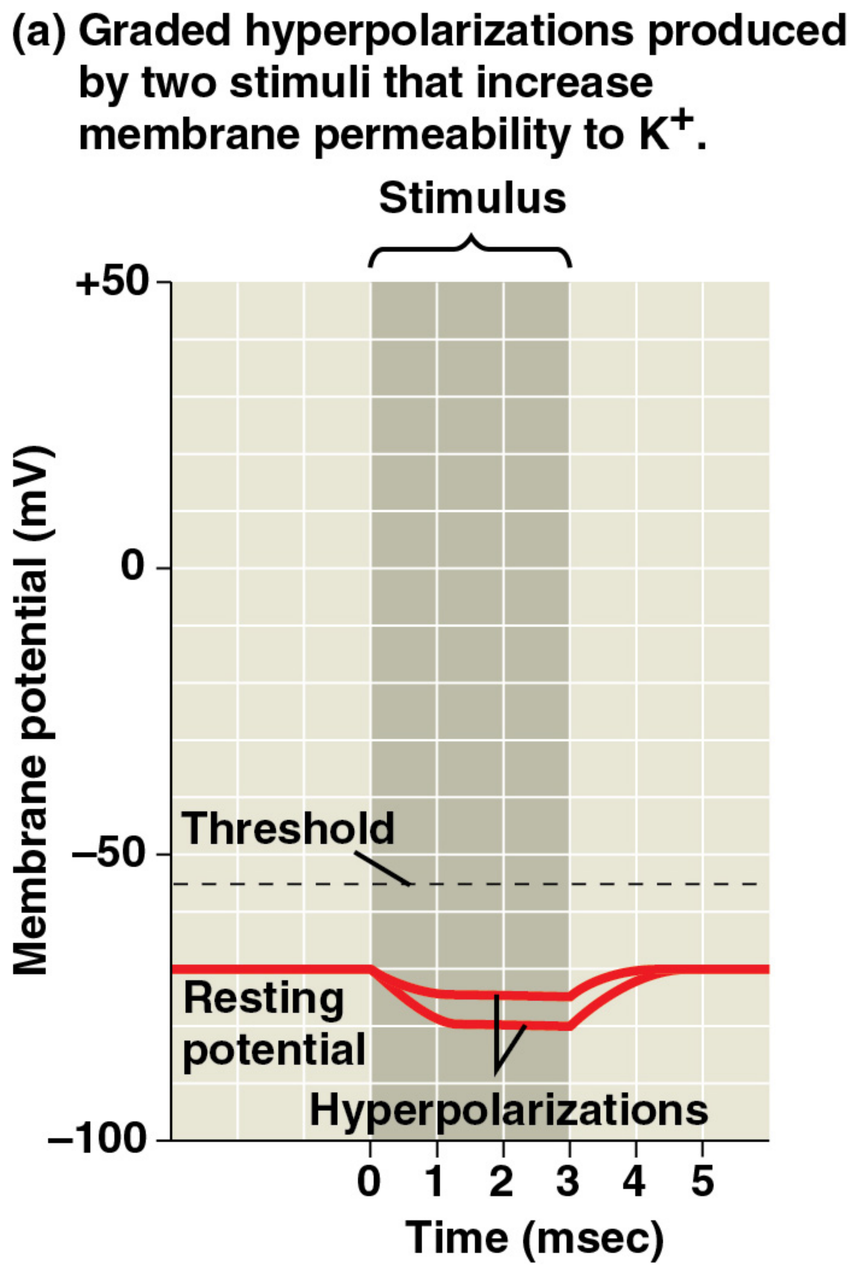
Gate closed: No ions flow across membrane.

Gate open: Ions flow through channel.

Hyperpolarization and Depolarization

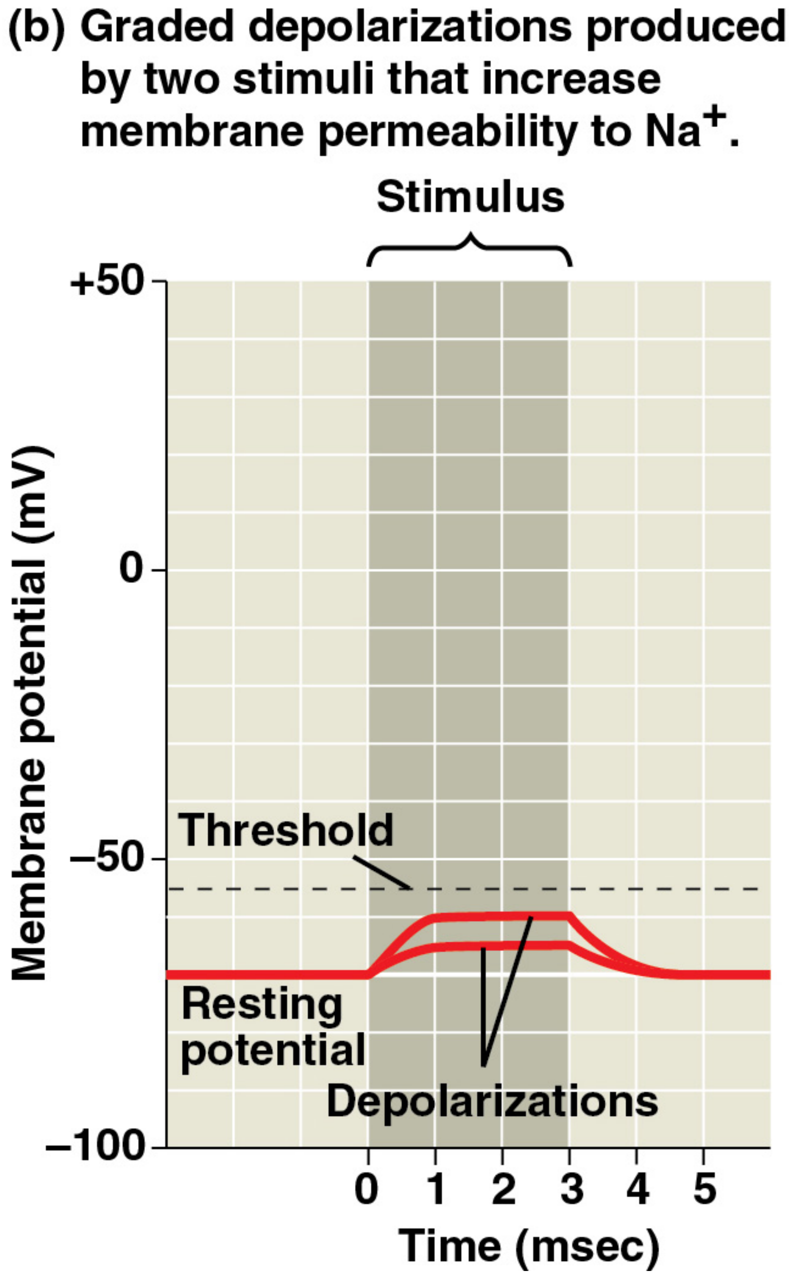
- When gated K^+ channels open, K^+ diffuses out, making the inside of the cell more negative
- This is **hyperpolarization**, an increase in magnitude of the membrane potential

Figure 48.11a



- Opening other types of ion channels triggers a **depolarization**, a reduction in the magnitude of the membrane potential
- For example, depolarization occurs if gated Na^+ channels open and Na^+ diffuses into the cell

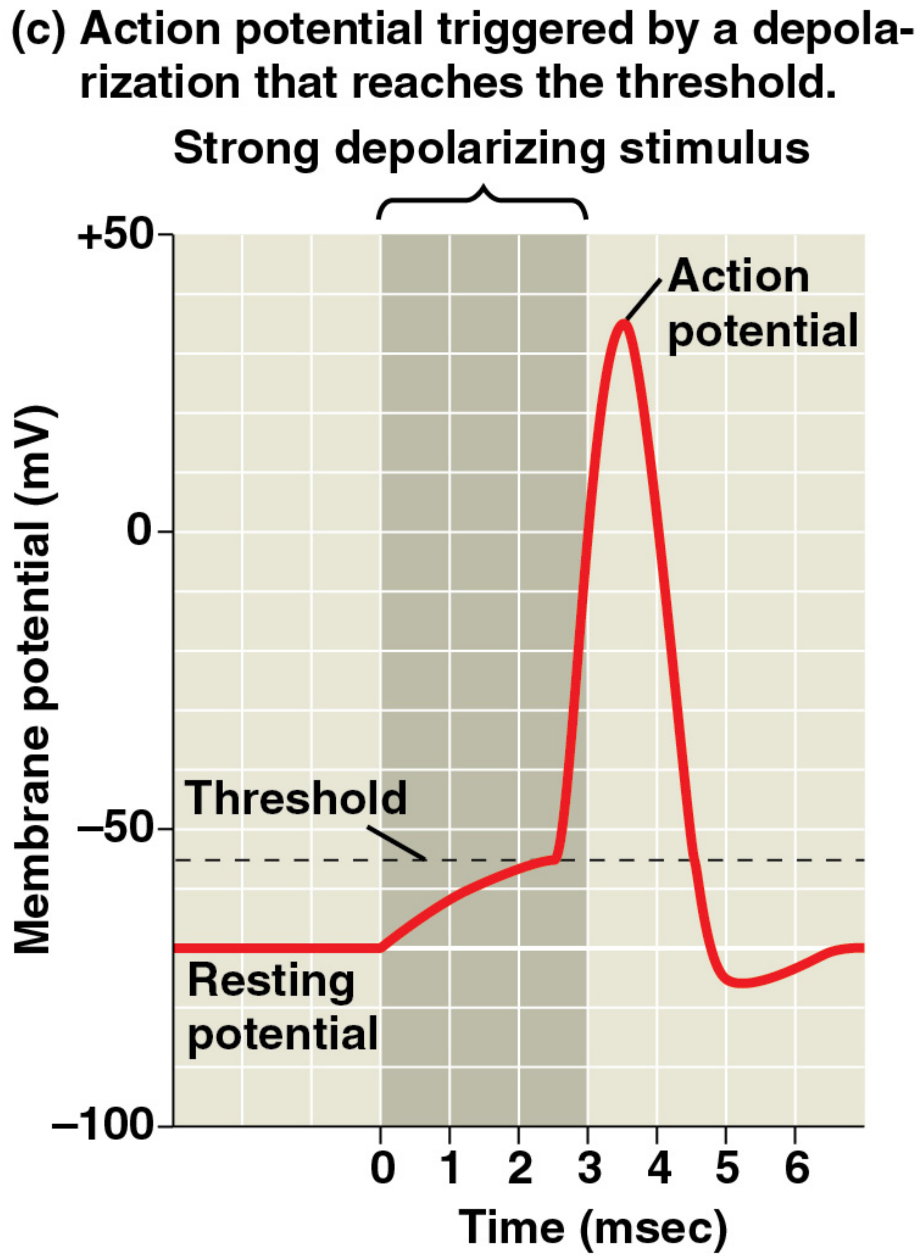
Figure 48.11b



Graded Potentials and Action Potentials

- **Graded potentials** are changes in polarization where the magnitude of the change varies with the strength of the stimulus
- If a depolarization shifts the membrane potential sufficiently, it results in a massive change in membrane voltage called an **action potential**

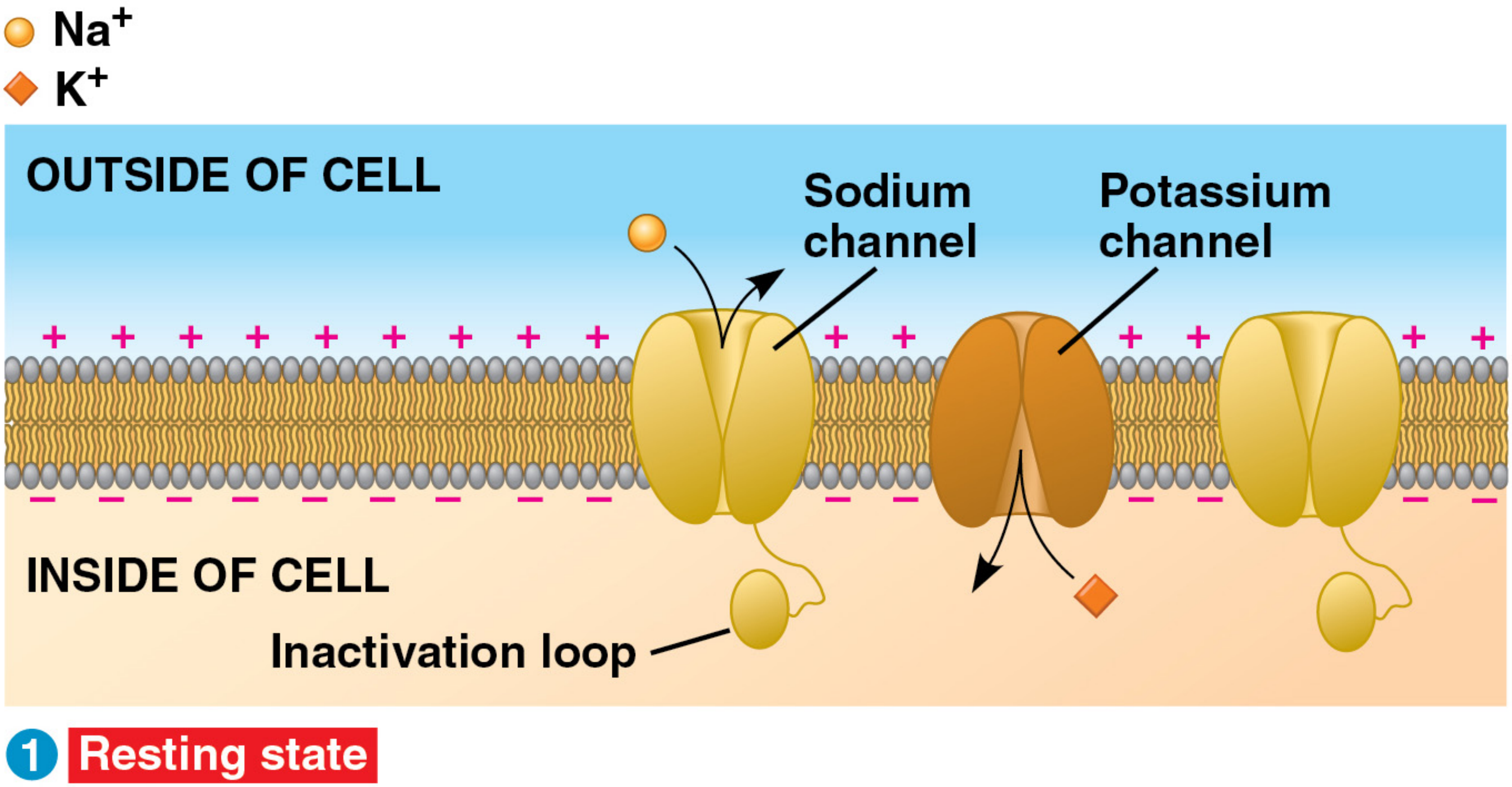
- Action potentials have a constant magnitude, are all-or-none, and transmit signals over long distances
- They arise because some ion channels are voltage-gated, opening or closing when the membrane potential passes a certain level called **threshold**


(c) Action potential triggered by a depolarization that reaches the threshold.
Strong depolarizing stimulus
+50
0
−50
−100
Membrane potential (mV)
Action potential
Threshold
Resting potential
0
1
2
3
4
5
6
Time (msec)

Generation of Action Potentials: *A Closer Look*

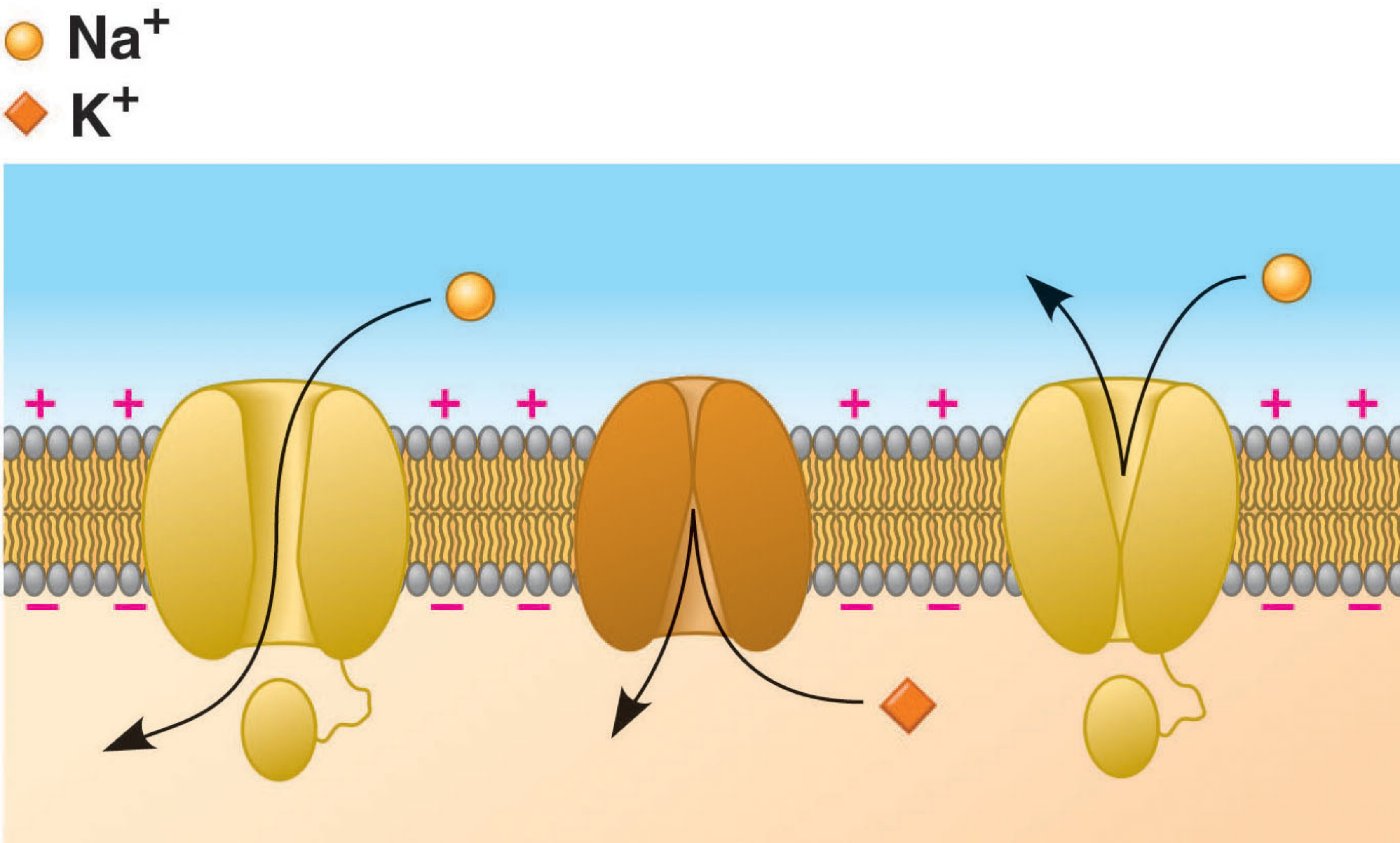
- An action potential results from changes in membrane potential as ions move through voltage-gated channels
- At resting potential
  1. Most voltage-gated sodium (Na^+) and potassium (K^+) channels are closed

Figure 48.12_1

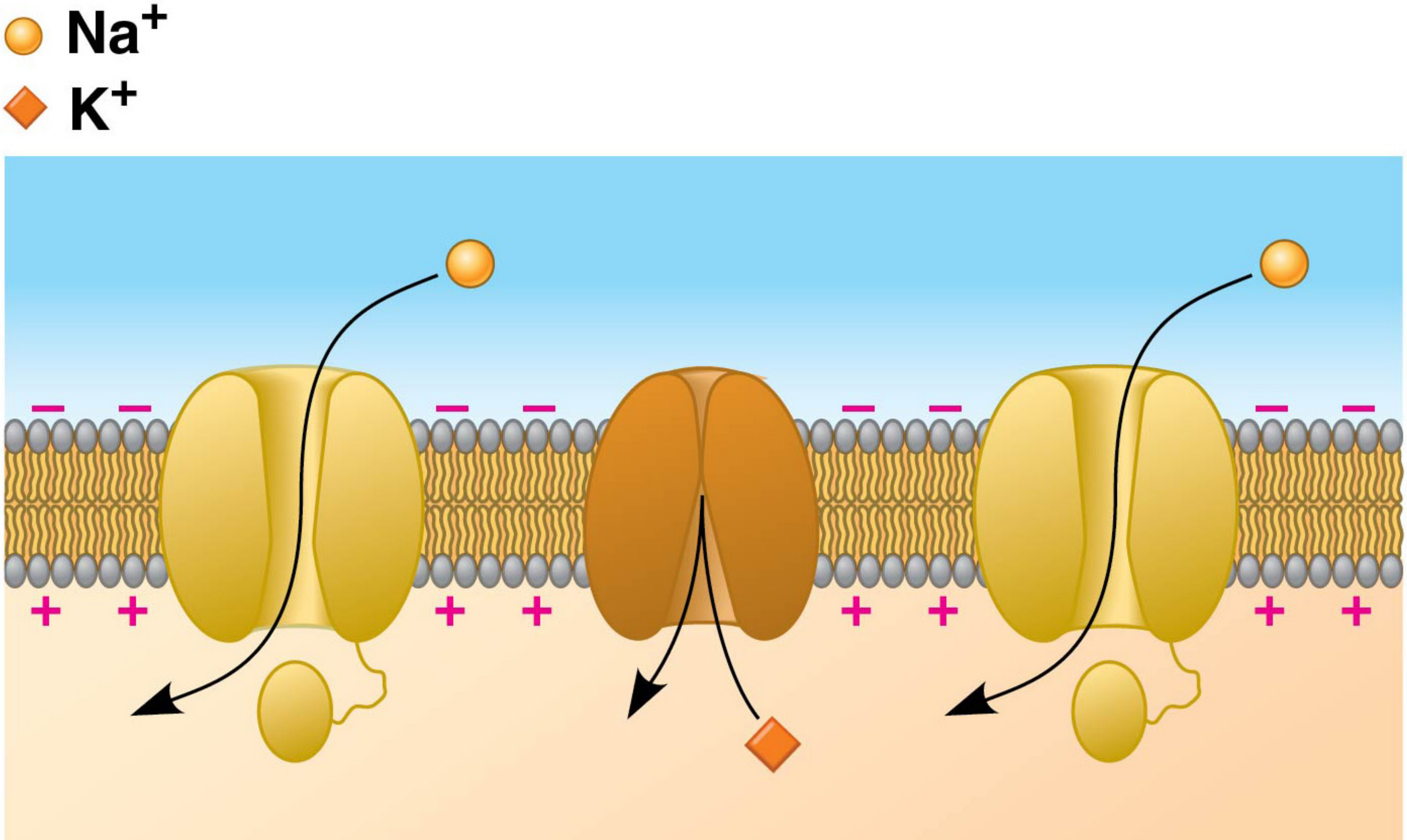


- When an action potential is generated,
  2. Voltage-gated Na^+ channels open first, and Na^+ flows into the cell
  3. During the rising phase, the threshold is crossed, the membrane potential increases close to E_{Na}
  4. During the falling phase, voltage-gated Na^+ channels become inactivated; voltage-gated K^+ channels open, and K^+ flows out of the cell

Figure 48.12_2

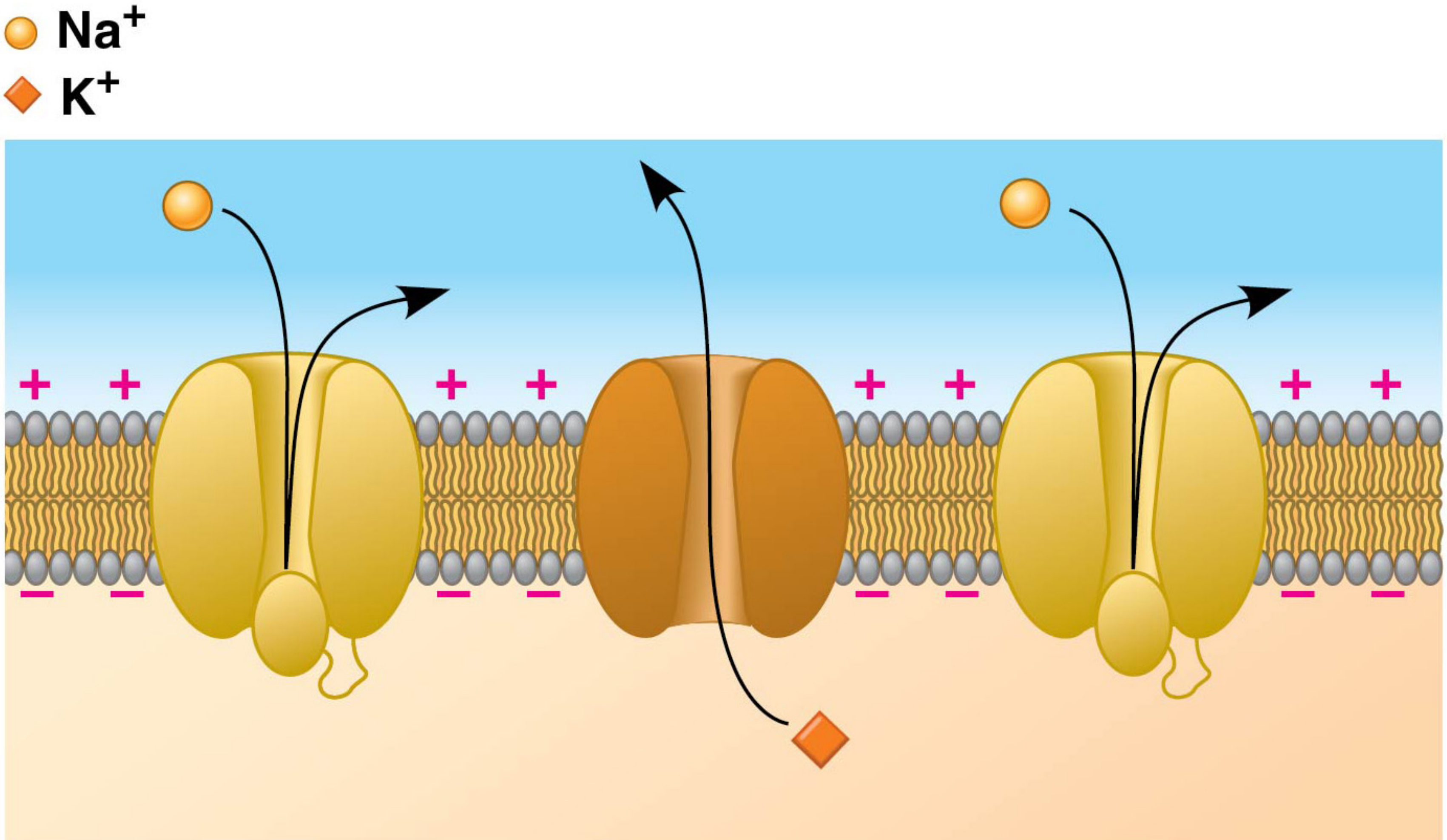


2 Depolarization



3 Rising phase of the action potential

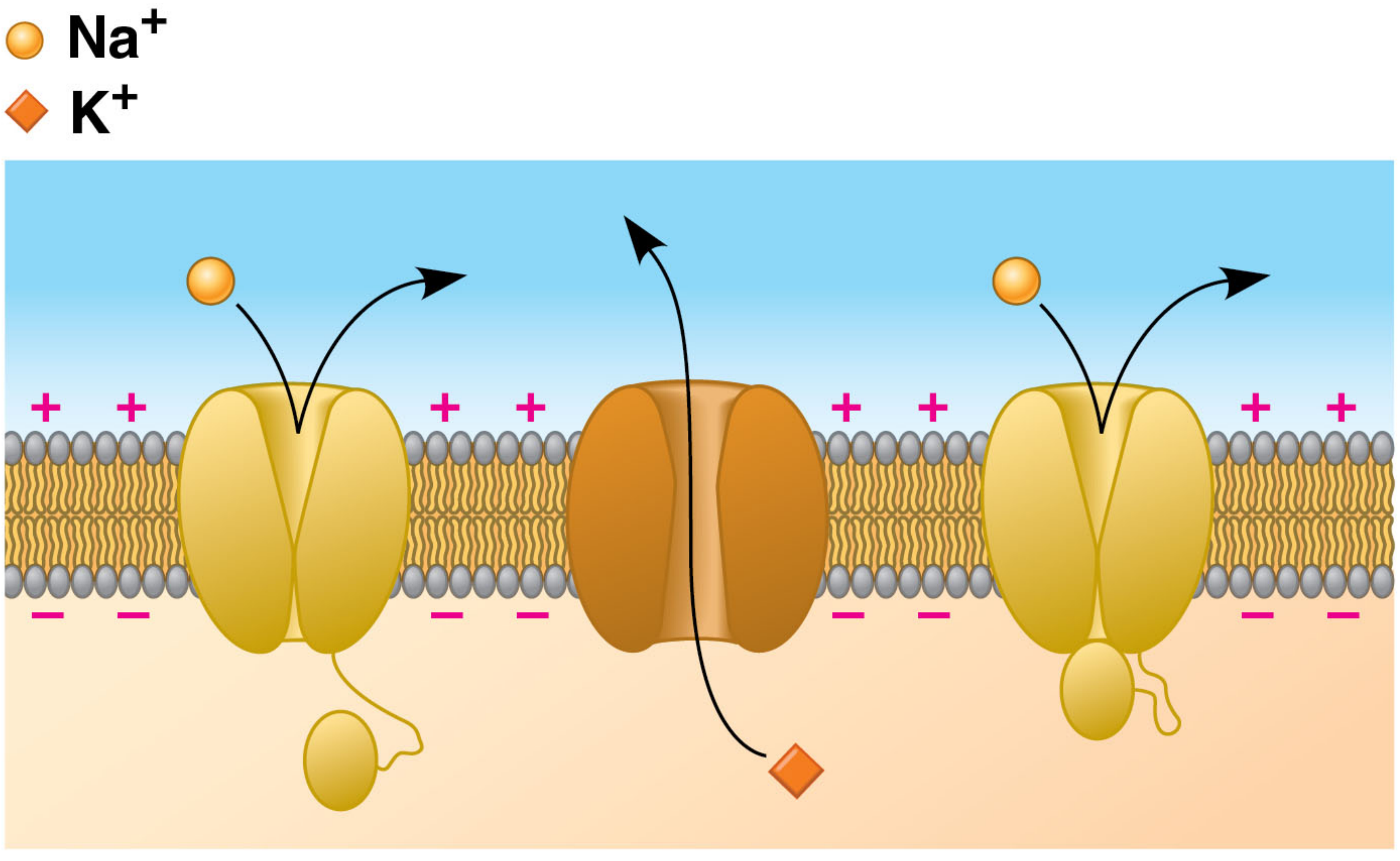
Figure 48.12_4



4 Falling phase of the action potential

5. During the undershoot, membrane permeability to K^+ is at first higher than at rest, then voltage-gated K^+ channels close and resting potential is restored

Figure 48.12_5



5 Undershoot

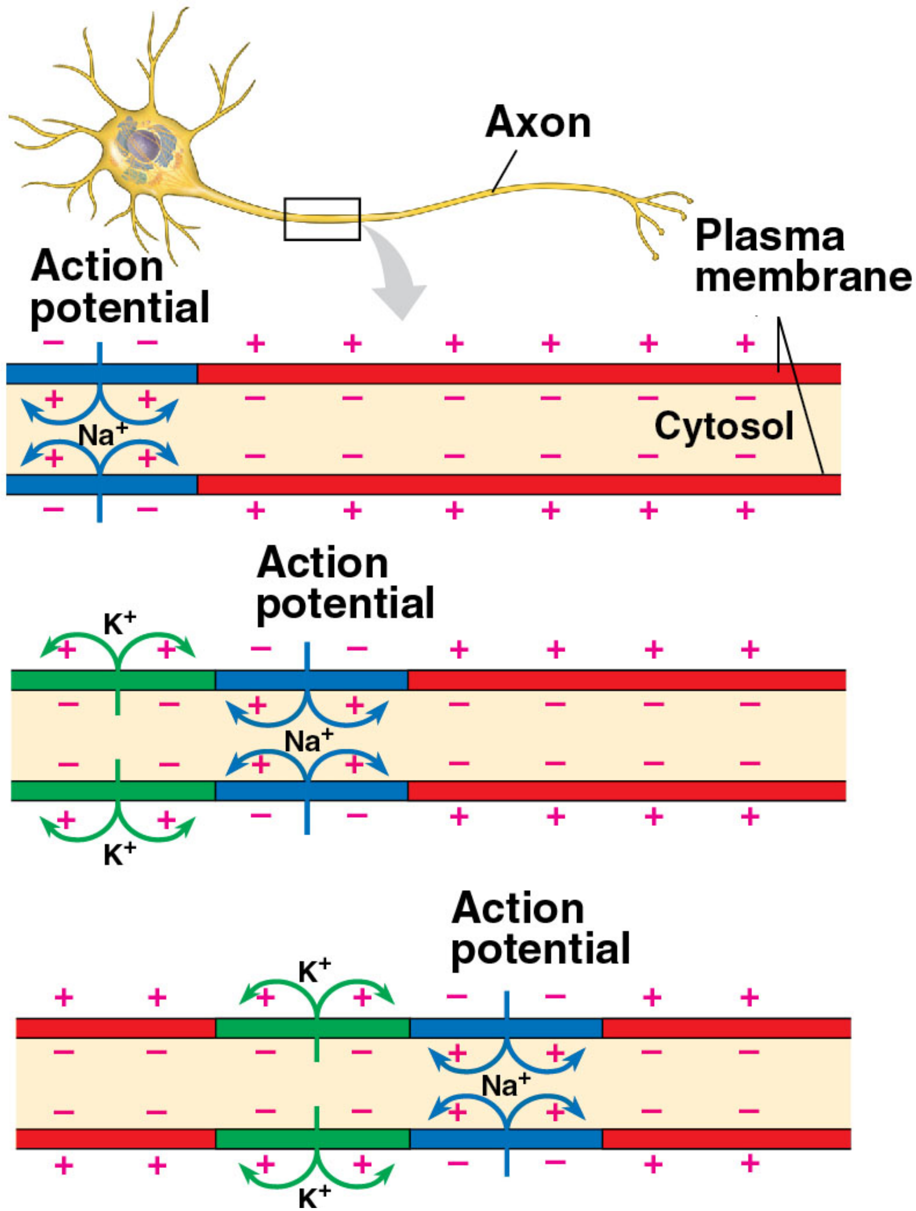
BioFlix® Animation: Action Potential

- During the **refractory period**, after an action potential, a second action potential cannot be initiated
- The refractory period is a result of a temporary inactivation of the Na^+ channels

Conduction of Action Potentials

- At the site where the action potential is generated (usually the axon hillock), an electrical current depolarizes the neighboring region of the axon membrane
- Action potentials are all-or-none and travel only toward the synaptic terminals
- Inactivated Na^+ channels behind the zone of depolarization prevent the action potential from traveling backwards

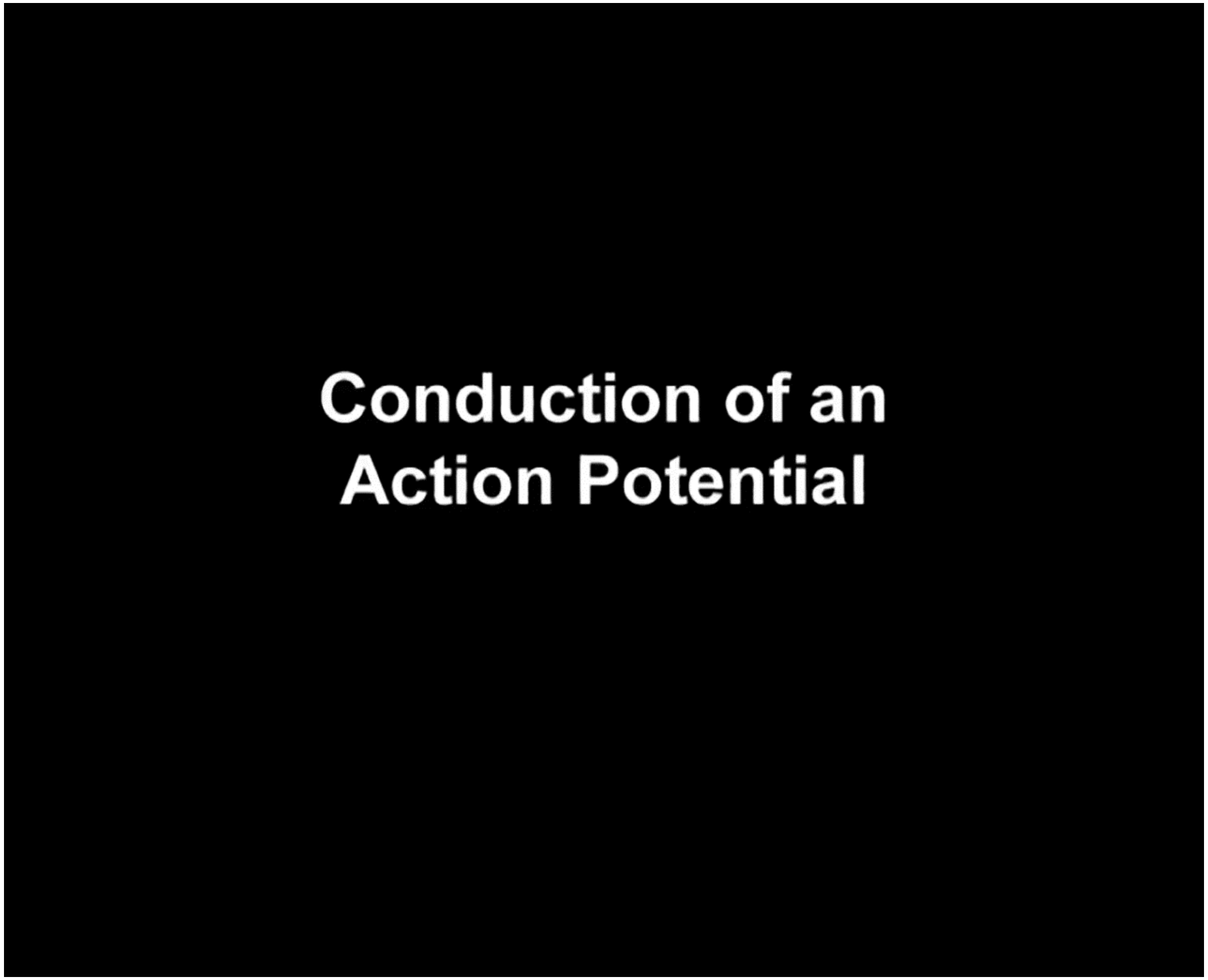
Figure 48.13



Axon
Plasma membrane
Action potential
Na+
Cytosol
Action potential
K+
Na+
K+
Action potential
K+
Na+
K+

- The rate at which action potentials are produced in a neuron is proportional to input signal strength
- Gated ion channels and action potentials play a central role in nervous system activity
- Mutations in genes that encode ion channels lead to disorders affecting the nerves or brain—or the muscles or heart

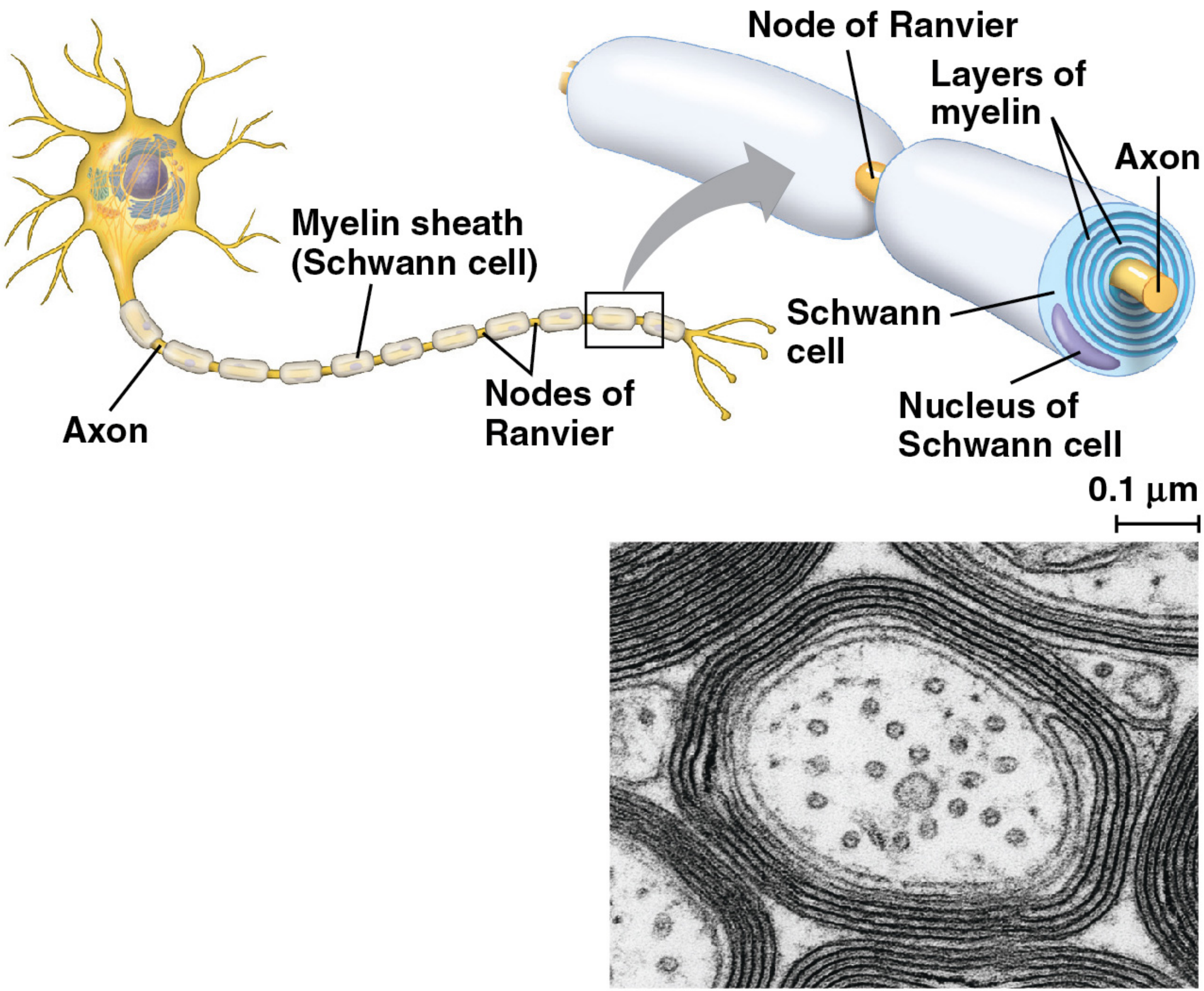
BioFlix® Animation: Conduction of an Action Potential



Evolutionary Adaptations of Axon Structure

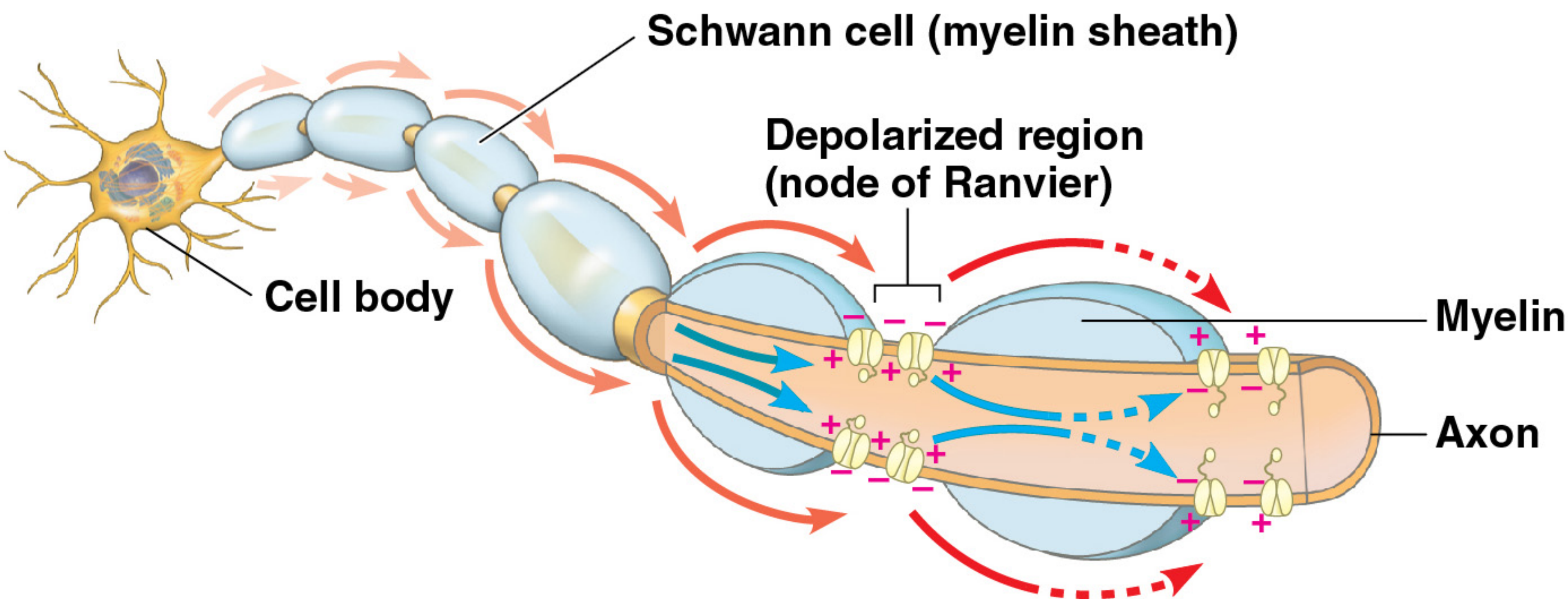
- The speed of an action potential increases with the axon’s diameter
- In vertebrates, axons are insulated by a **myelin sheath**, which causes an action potential’s speed to increase
- Myelin sheaths are made by glia—**oligodendrocytes** in the CNS and **Schwann cells** in the PNS

Figure 48.14


Node of Ranvier
Layers of myelin
Axon
Myelin sheath (Schwann cell)
Schwann cell
Nodes of Ranvier
Axon
Nucleus of Schwann cell
0.1 µm

- Voltage-gated sodium channels are restricted to **nodes of Ranvier**, gaps in the myelin sheath
- Action potentials in myelinated axons jump between the nodes of Ranvier in a process called **saltatory conduction**

Figure 48.15



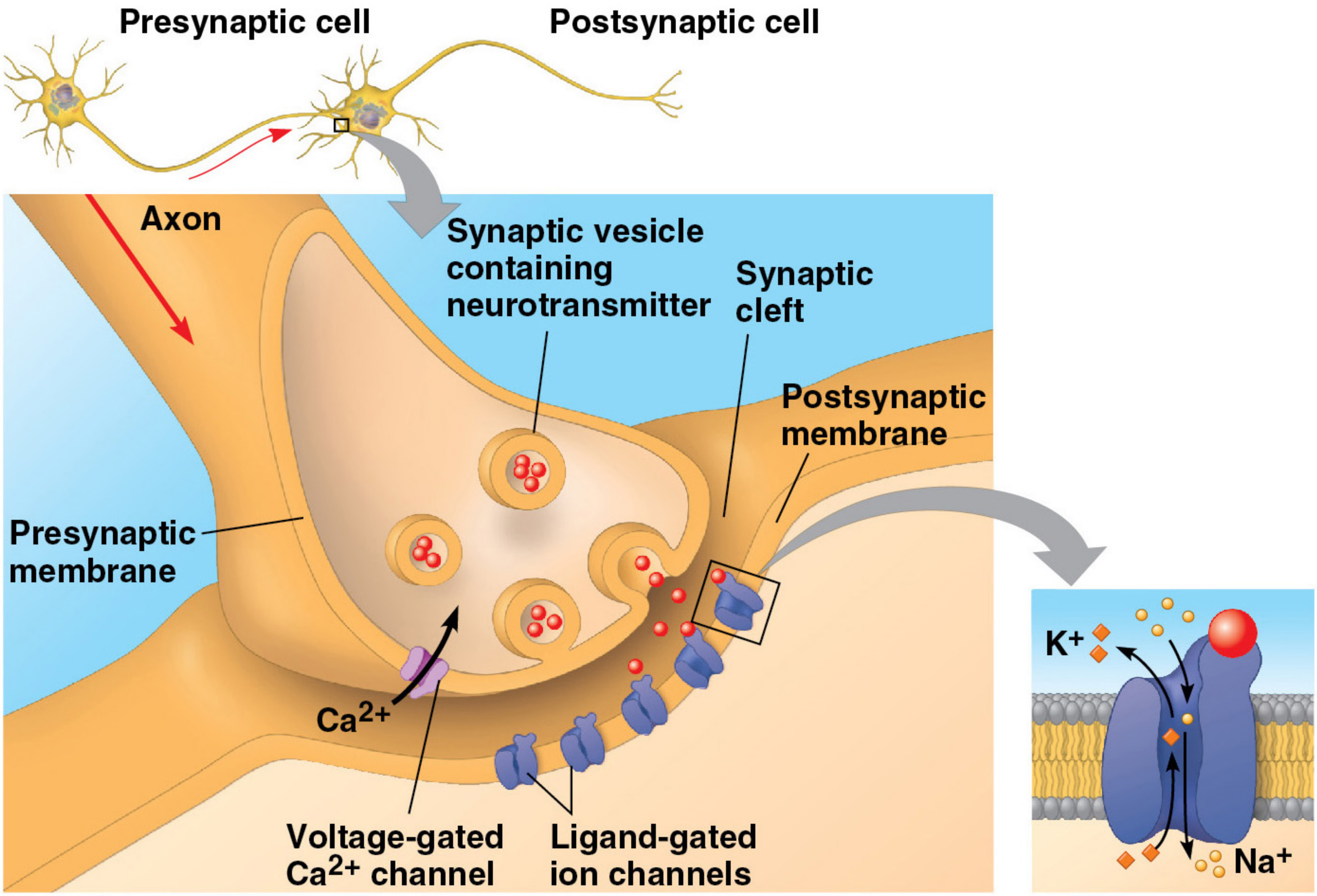
Schwann cell (myelin sheath)
Depolarized region
(node of Ranvier)
Cell body
Myelin
Axon

CONCEPT 48.4: Neurons communicate with other cells at synapses

- At electrical synapses, the electrical current flows from one neuron to another through gap junctions
- At chemical synapses, a chemical neurotransmitter carries information between neurons
- Most synapses are chemical synapses

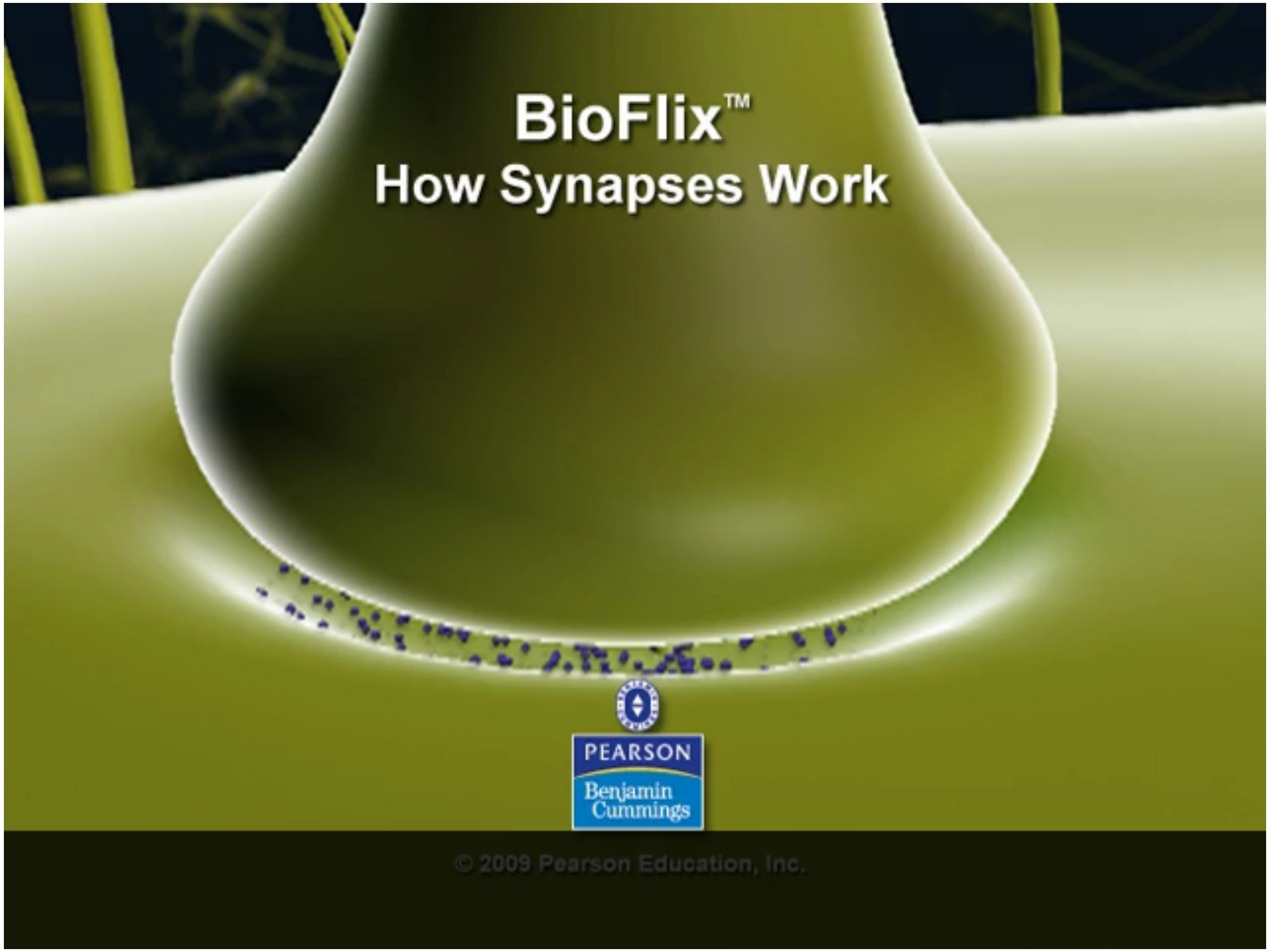
- The presynaptic neuron synthesizes and packages the neurotransmitter in synaptic vesicles located in the synaptic terminal
- The action potential causes the release of the neurotransmitter
- The neurotransmitter diffuses across the synaptic cleft and is received by the postsynaptic cell

Figure 48.16



Presynaptic cell
Postsynaptic cell
Axon
Synaptic vesicle containing neurotransmitter
Synaptic cleft
Postsynaptic membrane
Presynaptic membrane
Ca2+
Voltage-gated Ca2+ channel
Ligand-gated ion channels
K+
Na+

BioFlix® Animation: How Synapses Work



Generation of Postsynaptic Potentials

- At many chemical synapses, the receptor that binds and responds to neurotransmitters is a **ligand-gated ion channel**, often called an ionotropic receptor
- Neurotransmitter binding causes ion channels to open, generating a postsynaptic potential
- At some chemical synapses, the ligand-gated ion channels are permeable to both K^+ and Na^+

- Postsynaptic potentials fall into two categories
  - **Excitatory postsynaptic potentials (EPSPs)** are depolarizations that bring the membrane potential toward threshold
  - **Inhibitory postsynaptic potentials (IPSPs)** are hyperpolarizations that move the membrane potential farther from threshold

Summation of Postsynaptic Potentials

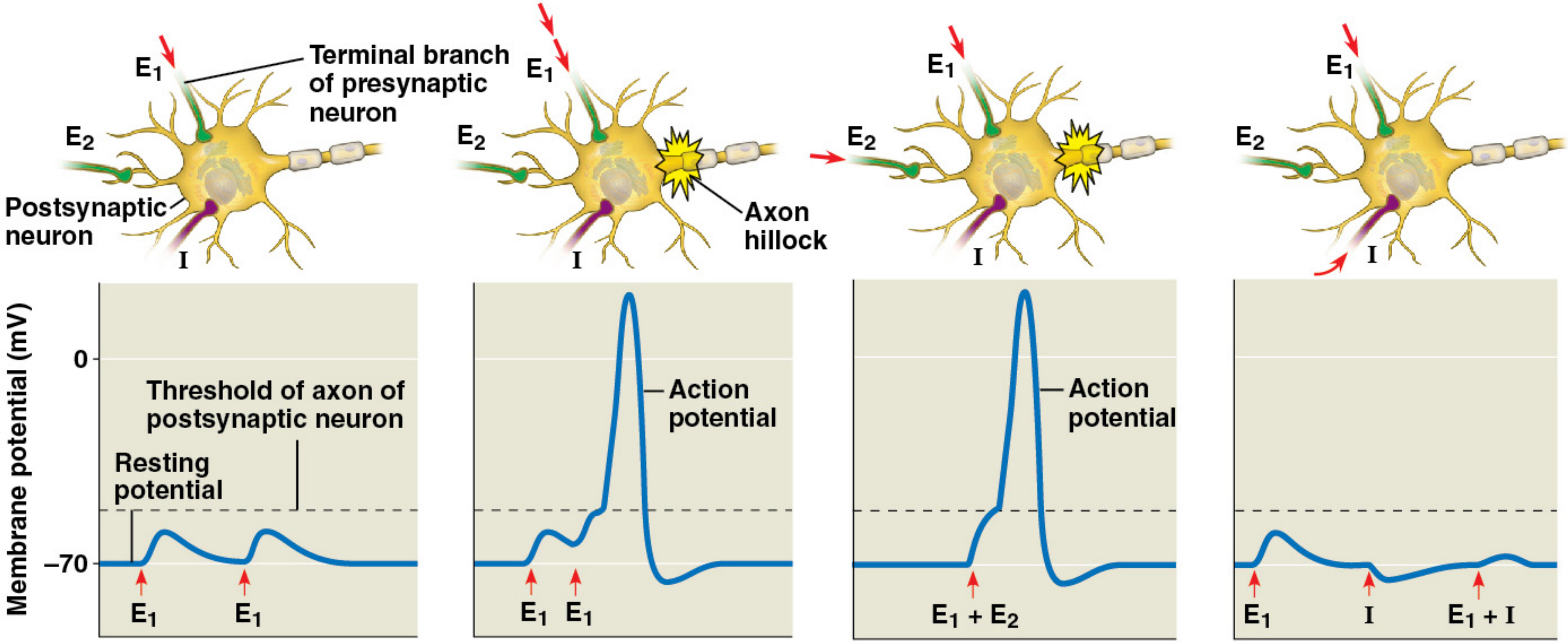
- The cell body and dendrites of a postsynaptic neuron may receive inputs from hundreds or thousands of synaptic terminals
- A single EPSP is usually too small to trigger an action potential in a postsynaptic neuron

- Individual postsynaptic potentials can combine to produce a larger potential in a process called **summation**
- If two EPSPs are produced in rapid succession, an effect called temporal summation occurs

- In spatial summation, EPSP s produced nearly simultaneously by different synapses on the same postsynaptic neuron add together
- The combination of EPSPs through spatial and temporal summation can trigger an action potential

- Through summation, an IPSP can counter the effect of an EPSP
- The summed effect of EPSPs and IPSPs determines whether an axon hillock will reach threshold and generate an action potential

Figure 48.17



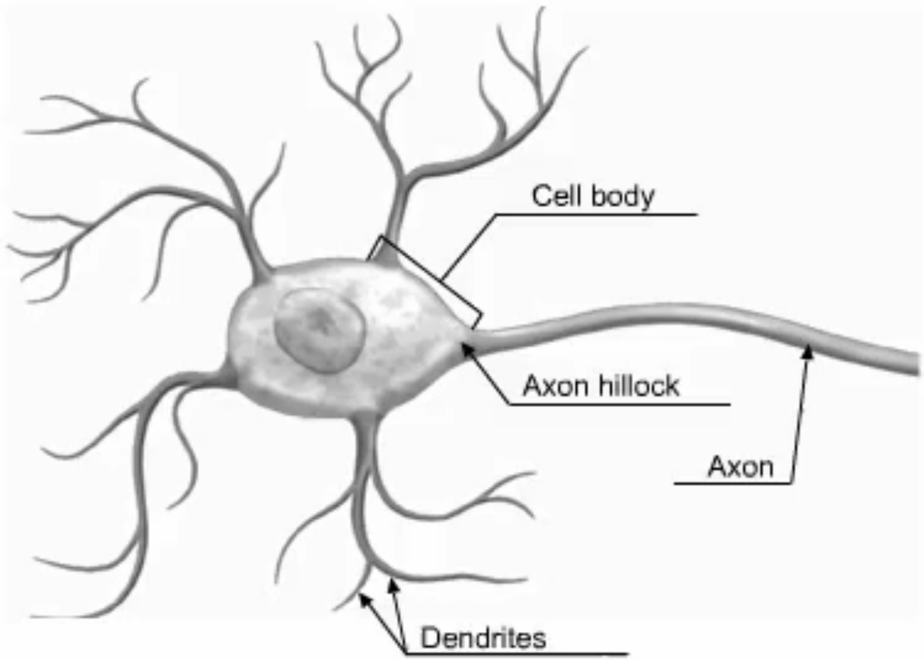
(a) Subthreshold, no summation

(b) Temporal summation

(c) Spatial summation

(d) Spatial summation of EPSP and IPSP

Animation: Action Potentials



Postsynaptic Potentials

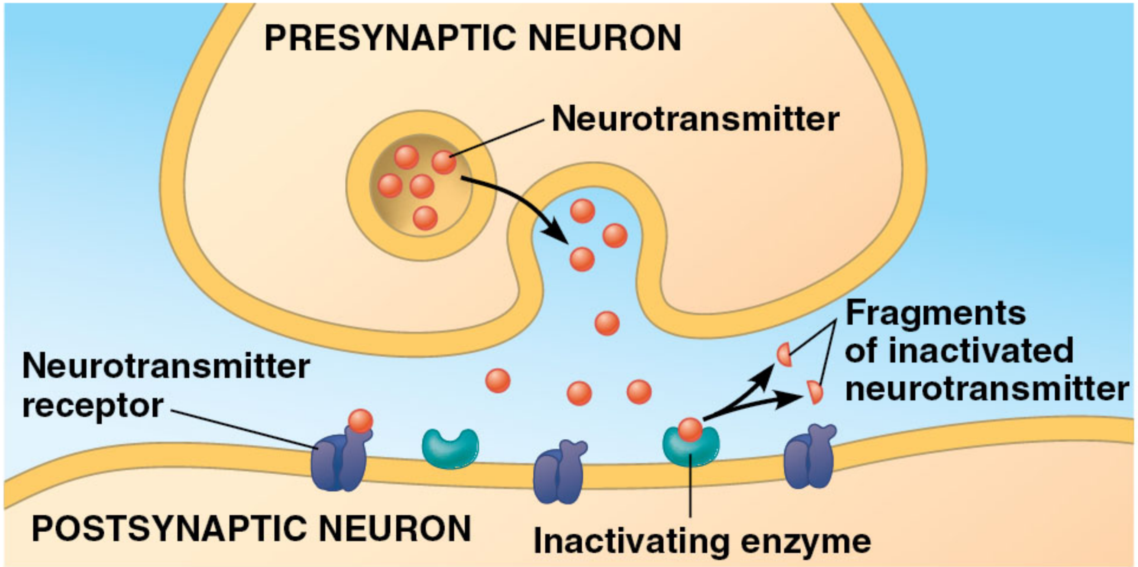
The *dendrites* and cell body of a *neuron* may receive thousands of synaptic connections from other neurons. When these neurons are activated, they release *neurotransmitters* that open *ligand-gated ion channels* in the membrane of the receiving neuron. As ions flow through these channels, the *membrane potential* of the receiving neuron changes at the point of stimulus and passively spreads along the membrane.

Termination of Neurotransmitter Signaling

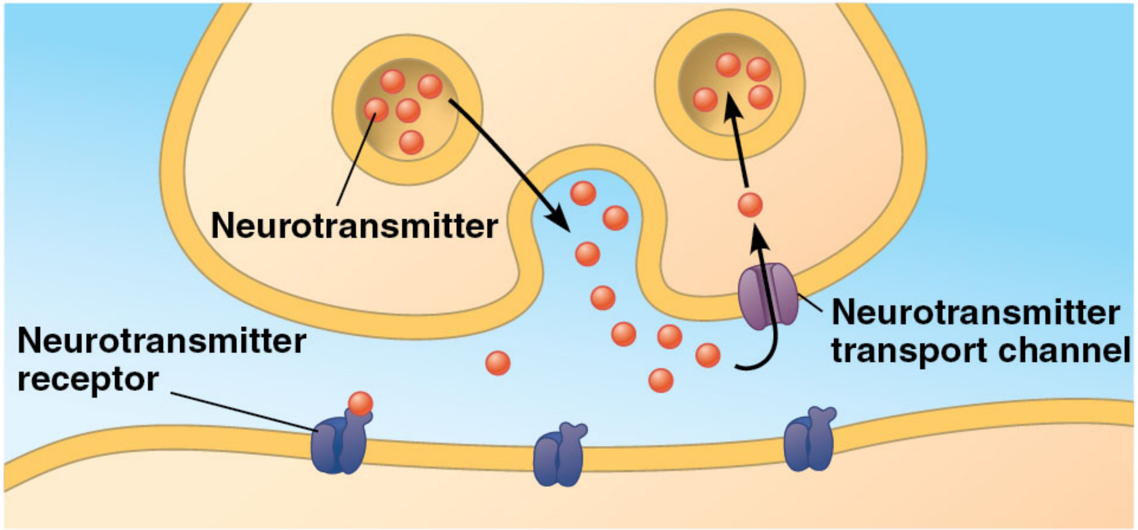
- After a response is triggered, the chemical synapse returns to its resting state
- The neurotransmitter molecules are cleared from the synaptic cleft
- Some are inactivated by enzymatic hydrolysis
- Others are recaptured into the presynaptic neuron

- Clearing neurotransmitter from the synaptic cleft is an essential step in nervous system transmission
- Blocking this process can have severe effects
- The nerve gas sarin triggers paralysis and death due to inhibition of the enzyme that breaks down the neurotransmitter controlling skeletal muscles

Figure 48.18



(a) Enzymatic breakdown of neurotransmitter in the synaptic cleft



(b) Reuptake of neurotransmitter by presynaptic neuron

Modulated Signaling at Synapses

- There are chemical synapses in which the receptor for the neurotransmitter is not part of an ion channel
- At these synapses, the neurotransmitter binds to a G protein-coupled receptor that is called metabotropic
- In this case, movement of ions through a channel depends on one or more metabolic steps

- Binding of a neurotransmitter to a metabotropic receptor activates a signal transduction pathway in the postsynaptic cell involving a second messenger
- The signal transduction pathway leads to amplification such that many channels can be opened or closed in response
- Many neurotransmitters have both ionotropic and metabotropic receptors

Neurotransmitters

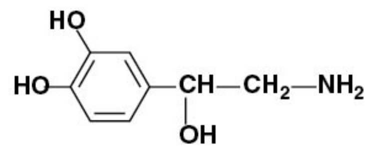
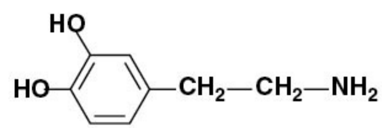
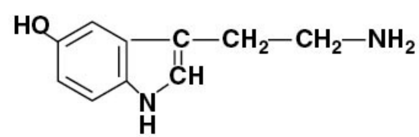
- A single neurotransmitter may bind specifically to more than a dozen different receptors
- A single neurotransmitter could excite postsynaptic cells expressing one receptor and inhibit postsynaptic cells expressing a different receptor
- **Acetylcholine** is a common neurotransmitter in vertebrates and invertebrates

Acetylcholine

- Acetylcholine is involved in muscle stimulation, memory formation, and learning
- Vertebrates have two major classes of acetylcholine receptor, one that is ligand gated and one that is metabotropic

- A number of toxins disrupt acetylcholine neurotransmission
- These include nicotine, the nerve gas sarin, and the botulinium toxin produced by certain bacteria
- Acetylcholine is just one of more than 100 known neurotransmitters
- The remainder fall into four classes: amino acids, biogenic amines, neuropeptides, and gases

Table 48.2

Neurotransmitter	Structure
Acetylcholine	$H_3C-\overset{\overset{\large O}{\Vert}}{C}-O-CH_2-CH_2-\overset{\overset{\large CH_3}{\vert}}{\underset{\underset{\large CH_3}{\vert}}{N^+}}-CH_3$
Amino Acids	
Glutamate	$H_2N-\underset{\underset{\large COOH}{\vert}}{CH}-CH_2-CH_2-COOH$
GABA (gamma-aminobutyric acid)	H_2N-CH_2-COOH
Glycine	$H_2N-CH_2-CH_2-CH_2-COOH$
Biogenic Amines	
Norepinephrine	
Dopamine	
Serotonin	
Neuropeptides (a very diverse group, only two of which are shown)	
Substance P	Arg—Pro—Lys—Pro—Gln—Gln—Phe—Phe—Gly—Leu—Met
Met-enkephalin (an endorphin)	Tyr—Gly—Gly—Phe—Met
Gases	
Nitric oxide	N=O

Amino Acids

- Glutamate is one of several amino acids that can act as a neurotransmitter in vertebrates and invertebrates
- Glycine acts at inhibitory synapses in parts of the CNS outside the brain
- Gamma-aminobutyric acid (GABA) is the neurotransmitter at most inhibitory synapses in the brain

Biogenic Amines

- Biogenic amines include norepinephrine, epinephrine, dopamine, and serotonin
- Norepinephrine is made from tyrosine
- Biogenic amines have a central role in a number of nervous system disorders
- Parkinson’s disease is associated with a lack of dopamine in the brain

Neuropeptides

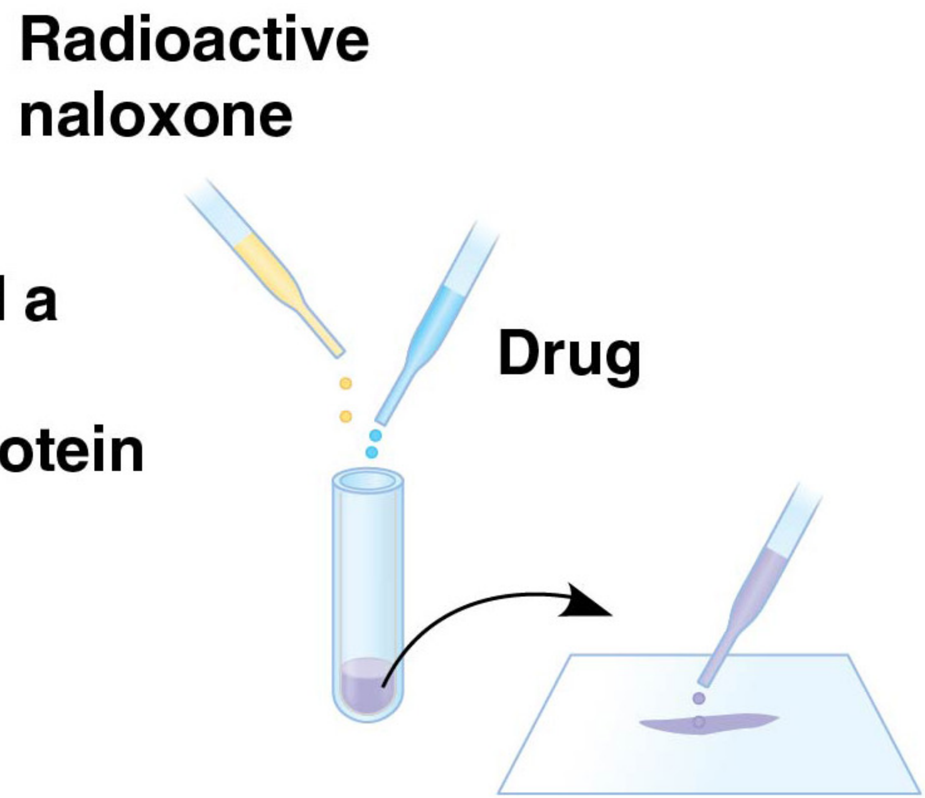
- Several **neuropeptides**, relatively short chains of amino acids, also function as neurotransmitters
- Neuropeptides include substance P, and **endorphins**, which both affect our perception of pain
- Opiates bind to the same receptors as endorphins and can be used as painkillers

Gases

- Gases such as nitric oxide (NO) are local regulators in the PNS
- Unlike most neurotransmitters, NO is not stored in cytoplasmic vesicles, but is synthesized on demand
- It is broken down within a few seconds of production

- Although inhaling CO can be deadly, the vertebrate body synthesizes small amounts of it, some of which is used as a neurotransmitter

Figure 48.UN01



1 Radioactive naloxone and a test drug are added to a protein mixture.

2 Proteins are trapped on a filter. Bound naloxone is detected by measuring radioactivity.

Figure 48.UN01

Drug	Opiate	Lowest Concentration That Blocked Naloxone Binding
Morphine	Yes	6×10^{-9} *M*
Methadone	Yes	2×10^{-8} *M*
Levorphanol	Yes	2×10^{-9} *M*
Phenobarbital	No	No effect at 10^{-4} *M*
Atropine	No	No effect at 10^{-4} *M*
Serotonin	No	No effect at 10^{-4} *M*

Data from C. B. Pert and S. H. Snyder, Opiate receptor: demonstration in nervous tissue, *Science* 179:1011–1014 (1973).

Figure 48.UN02

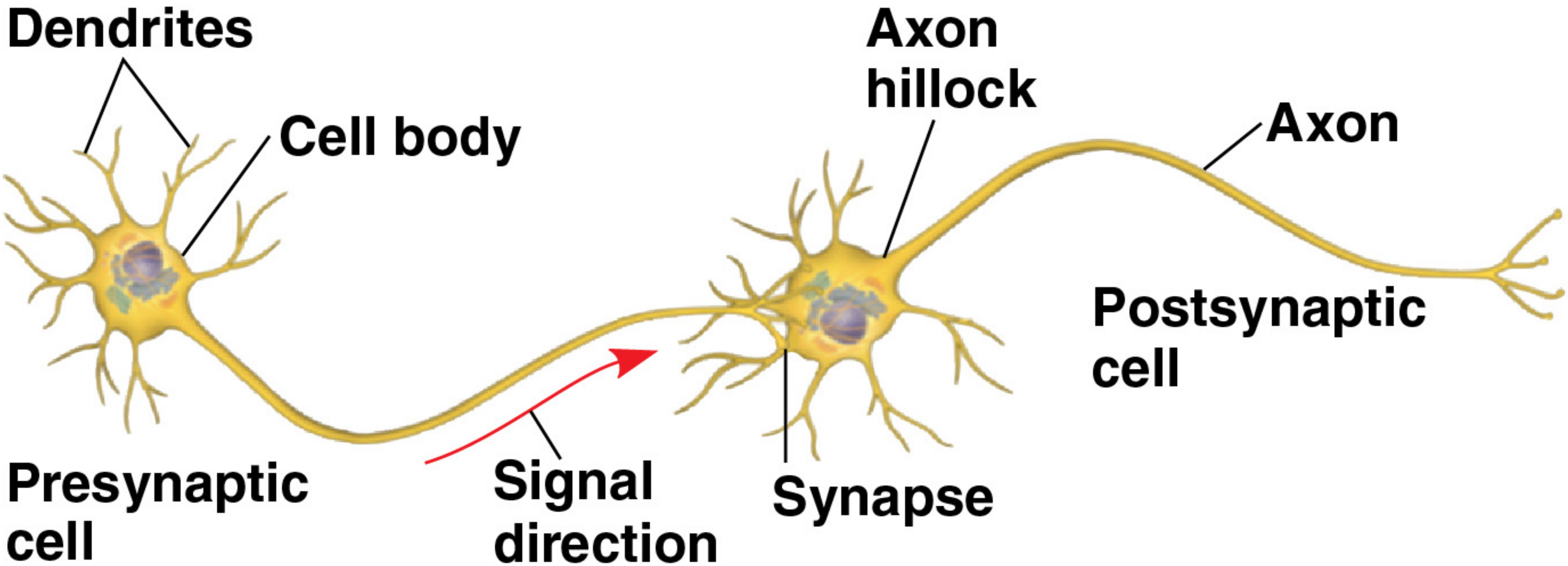


Figure 48.UN03

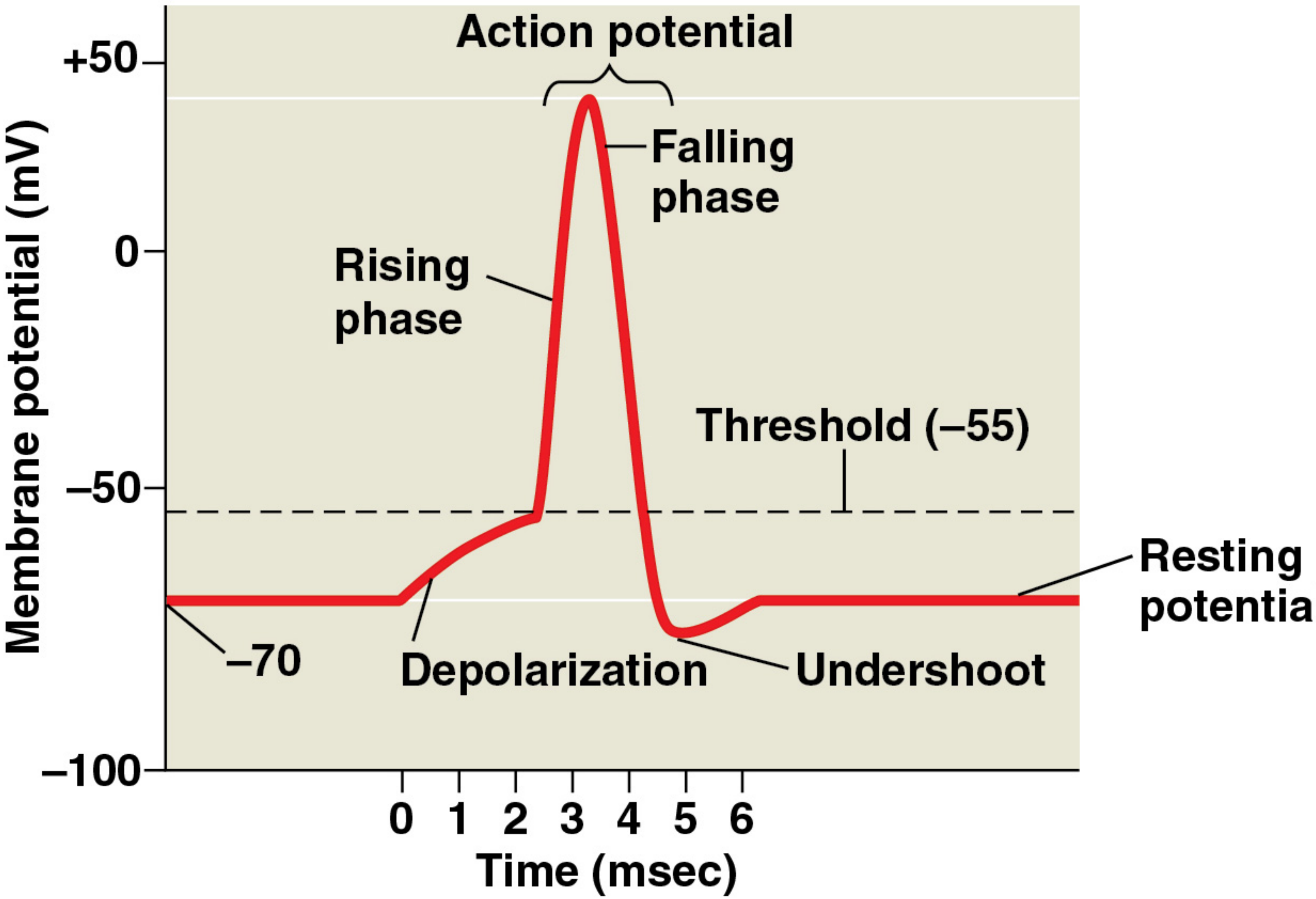


Figure 48.UN04

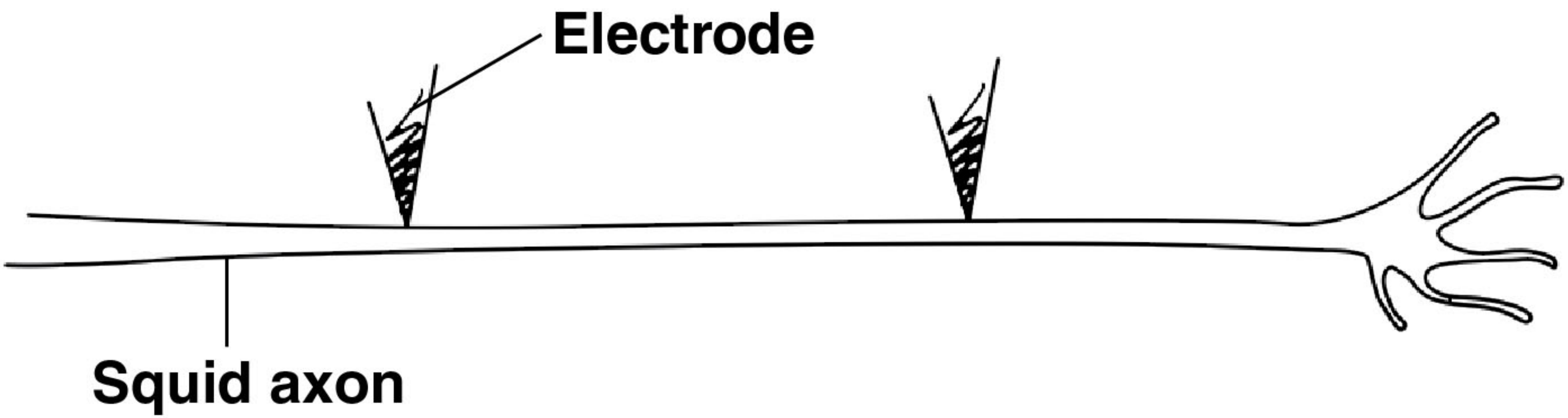


Figure 48.UN05